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(54) Title: NOVEL BACTERIAL GENES AND PROTEINS THAT ARE ESSENTIAL FOR CELL VIABILITY AND THEIR  
USES

(57) Abstract: The present invention provides novel bacterial genes and their encoded polypeptides thereof which are essential for  
bacterial cell viability, and their uses.

# NOVEL BACTERIAL GENES AND PROTEINS THAT ARE ESSENTIAL FOR CELL VIABILITY AND THEIR USES

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10 Throughout this application various publications are referenced. The disclosures of these publications in their entireties are hereby incorporated by reference into this application in order to more fully describe the state of the art to which this invention pertains.

## FIELD OF THE INVENTION

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The present invention relates generally to nucleotide sequences, and polypeptides encoded by the sequences, that are essential for bacterial viability, and to methods of using the nucleotide and polypeptide sequences.

## 20 BACKGROUND OF THE INVENTION

Bacterial genera, such as *Streptococcus*, *Staphylococcus*, *Pseudomonas*, *Yersinia*, *Salmonella*, and *Enterobacter*, are the cause of numerous afflictions in humans and animals. Bacterial infection can lead to serious health conditions, including pneumonia, 25 osteomyelitis, meningitis, sinusitis, otitis, cystitis, and even food poisoning. Typically, these infections can be treated with standard antimicrobial agents such as antibiotics. However, the emergence of pathogenic bacterial strains that are resistant to antibiotics has risen alarmingly in the past two decades. This situation has created an urgent need for the development of new antimicrobial agents.

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One strategy for developing new antimicrobial agents is to identify bacterial gene sequences that encode gene products that are essential for bacterial cell viability and



develop and/or identify agents which inhibit the function of the gene product. DNA sequencing technology has advanced from sequencing one gene at a time to sequencing entire genomes, the sum of all genes in an organism. With the recent arrival of bacterial genomic information, it is now possible to compare multiple bacterial genomes in an attempt to identify genes that encode conserved gene products. In this manner, one skilled in the art may identify a set of conserved bacterial genes, including a subset of genes that are essential for bacterial cell viability. The essential gene is then used as a starting point to develop therapeutic agents that inhibit or inactivate the product of the essential gene.

The availability of DNA sequence information for multiple microbial genomes is a recent development. The public release of the first complete genome, *Haemophilus influenzae* (Fleischmann, R.D., et al. 1995 *Science* 269:496-512), was followed in rapid succession by a number of public and private genome sequencing programs. Presently, some 20 completely sequenced bacterial genomes have been published, and over 100 other sequencing projects are underway (Blattner, F.R., et al., 1997 *Science* 277:1453-74; Ferretti, J.J., et al., 1997 *Adv Exp Med Biol* 418:961-963; Koonin, E.V., et al., 1996 *Methods Enzymol* 266:295-322). Analyses of these data indicate that approximately 46% of putative bacterial genes are of unknown function having no attributable function.

Others have pursued various strategies to identify bacterial genes that are essential for viability. These strategies include: identifying genes that are expressed by the bacteria when present in the infected host (Hensel, M., et al., 1995 *Science* 269:400-3), identifying essential genes by isolating temperature sensitive mutants (Schmid, M.B., et al., 1998 *Curr Opin Chem Biol* 2:529-34), and identifying genes in pathways known from prior physiological studies to be essential (Skarzynski, T. et al., 1996 *Structure* 1996 4:1465-74)

There continues to be a need to identify bacterial genes that encode gene products that are essential for cell viability, such as cell replication, growth, and survival. These genes and their encoded gene products can be used as a starting point towards identifying agents

that inhibit functions essential for cell viability, thereby causing bacterial cell stasis or death (e.g., antibacterial agents).

5 The present invention provides experimental identification of novel, conserved essential genes (*ceg*) from bacteria and their encoded protein products. The *ceg* genes are considered essential to cell viability because disruption of an endogenous *ceg* gene results in lethality of a bacterial cell (e.g., as determined by failure to recover viable chloramphenicol-resistant colonies, as described herein). Thus, the gene products encoded by these genes are potentially valuable targets for chemotherapeutic intervention  
10 of bacterial infections.

The *ceg* nucleotide sequences of the invention were obtained by large-scale computational comparisons of multiple genome sequences to identify conserved protein coding regions, followed by gene disruption to identify *cegs*. The conservation of protein  
15 sequences in many cases is believed to reflect the higher level conservation of common biochemical pathways essential for bacterial function and viability.

#### SUMMARY OF THE INVENTION

20 The acronyms "CEG" and "*ceg*" stand for Conserved Essential Gene. For convenience, the italicized term *ceg* refers herein to *ceg* nucleotide sequences. The capitalized term CEG refers herein to CEG polypeptide sequences.

Embodiments of the *ceg* nucleotide sequences and the CEG polypeptide sequences are  
25 designated CFEs which stands for CEG For Expression. The CFEs are polypeptides resulting from expression of the *ceg* nucleotide sequence.

The present invention provides isolated nucleotide sequences of conserved essential genes from bacteria, designated *ceg*. The invention also provides recombinant nucleic  
30 acid molecules including the *ceg* sequences of the invention, and methods of uses thereof. Examples of nucleic acid molecules having *ceg* sequences are described in SEQ ID

NOS.: 1-113. The invention further provides isolated polypeptides and recombinant polypeptides having the CEG sequences of the invention, and methods of uses thereof. Examples of polypeptides having CEG sequences are described in SEQ ID NOS.:114-226.

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The *ceg* sequences of the present invention are DNA or RNA. Further, the invention includes nucleic acid molecules that are identical or nearly identical (e.g., similar) with the *ceg* sequences of the invention. The invention additionally provides polynucleotide sequences that hybridize under stringent conditions to the *ceg* sequences of the invention.

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A further embodiment provides polynucleotide sequences which are complementary to the *ceg* sequences of the invention. Yet another embodiment provides *ceg* nucleic acid molecules that are labeled with a detectable marker. Another embodiment provides recombinant nucleic acid molecules, such as a vector or a fusion molecule, including the *ceg* sequences of the invention.

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The present invention provides various *ceg* sequences, fragments thereof having essential gene activity, and related molecules such as antisense molecules, oligonucleotides, peptide nucleic acids (PNA), fragments, and portions thereof.

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The present invention relates to the inclusion of the polynucleotides encoding CEG gene products, such as CEG polypeptides, in an expression vector which can be used to transform host cells or organisms. Such transgenic hosts are useful for the production of CEG gene products for the development of antibacterial agents such as antibiotics.

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The invention further provides substantially purified CEG gene products, and uses thereof.

The invention also relates to pharmaceutical compositions comprising antisense molecules capable of disrupting expression of *ceg* sequences, agonists, antagonists or inhibitors of CEG gene products, and antibodies reactive against the CEG polypeptides.

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These compositions are useful for preventing the growth or survival of bacteria, for example, in the treatment of conditions associated with bacterial infections.

### BRIEF DESCRIPTION OF THE FIGURES

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Figure 1: A schematic representation of the gene disruption assay, as described in Example 3, *infra*. A) A recombinant vector undergoing homologous recombination with the host genome. B) The result of homologous recombination.

- 10 Figure 2: A schematic representation of the polarity test for operons, as described in Examples 2 and 3, *infra*. A) The recombinant vector undergoing homologous recombination with the host genome. B) Case 1: one possible result of homologous recombination; the downstream Gene B has an independent promoter. C) Case 2; another possible result of homologous recombination; the downstream Gene B does not have an independent promoter.
- 15

- Figure 3: Purification of 2CFE 75, as described in Example 6, *infra*. A) Fractionation profile of 2CFE 75 eluted from a Ni-NTA column. B) Gel electrophoresis of pooled fractions of CFE 75. C) Non-denaturing gel electrophoresis to determine oligo form of
- 20 2CFE 75.

Figure 4: Fractionation profile of 2CFE 3 eluted from a hydroxyapatite column, as described in Example 7, *infra*.

- 25 Figure 5: The biosynthesis pathway of Coenzyme A which starts with phosphorylation of pantothenate.

- Figure 6: Circular dichroism spectra of 2CFE 101 and 103, as described in Example 10, *infra*. A) Circular dichroism spectra of 2CFE 101 and 103 at 25 degrees C. B) Circular
- 30 dichroism thermal melt spectra of 2CFE 101 and 103 at a range of zero to 100 degrees C.

Figure 7: Circular dichroism spectra of aggregate and monomer pools of 2CFE 101 and 103, as described in Example 10, *infra*. A) Circular dichroism spectra of aggregate and monomer pools of 2CFE 101 and 103 at 25 degrees C. B) Circular dichroism thermal melt spectra of aggregate and monomer pools of 2CFE 101 and 103 at a range of zero to 100 degrees C.

5

Figure 8: Absorbance spectra of pantothenate-dependent production of ADP, as described in Example 10, *infra*.

Figure 9: The results of size exclusion chromatography and gel electrophoresis showing the oligomeric forms of 2CFE 21 and 39, as described in Example 11, *infra*. Lanes 1-6 contain 2CFE 21, lane 7 is a molecular weight marker, lanes 8-10 contain 2CFE 39.

Figure 10: Gel electrophoresis of a helicase reaction using 2CFE 21 and 39 and radiolabeled synthetic Holliday Junction template, as described in Example 11, *infra*. Lane 1 contains the synthetic Holliday Junction template; lane 2 contains the synthetic duplex; lane 3 contains a single-stranded template; lane 4 contains the helicase reaction using 2CFE 39; lane 5 contains the helicase reaction using 2CFE 21; lanes 6-8 contain the helicase reaction using 2CFE 39 and 21 at varying concentrations (e.g., 1, 2, and 3  $\mu$ M each); and lane 9 contains the helicase reaction using 2  $\mu$ M each 2CFE 39 and 21 in the presence of ethidium bromide.

20

Figure 11: A graph depicting the results of the helicase reaction which were monitored by measuring the unquenching of the Holliday Junction templates with time, as described in Example 11, *infra*.

25

Figure 12: Capillary electrophoresis results of 2CFE 8 with and without ssDNA, as described in Example 12, *infra*. A) Electropherogram of 2CFE 8 alone. B) Electropherogram of 2CFE 8 in the presence of a 32-nucleotide single-stranded oligomer.

Figure 13: Gel mobility shift assay of 2CFE 8, and 2CFE 8 in the presence of a single-stranded 32-mer, as described in Example 12, *infra*. A) An ethidium bromide-stained,

30

native, polyacrylamide gel containing 2CFE 8, and 2CFE 8 in the presence of a 32-mer. B) The same native, polyacrylamide gel stained with Coomassie.

Figure 14: The N-acetyl glucosamine pathway putatively mediated by 2CFE 3 and 2CFE 86, as described in Example 13, *infra*.

Figure 15: Capillary electrophoresis results of 2CFE 3 with and without putative substrates, as described in Example 13, *infra*. A) Electropherogram of 2CFE 3 with and without glucosamine-1-phosphate. B) Electropherogram of 2CFE 3 with and without D-glucose-1-phosphate. C) Electropherogram of 2CFE 3 alone, 2CFE 3 and glucose-1-phosphate, and 2CFE 3 and glucose-6-phosphate. D) Electropherogram of 2CFE 3 alone or in the presence of glucosamine-1-phosphate, glucosamine-6-phosphate, D-glucose, D(+) galactose, and  $\alpha$ -D-glucose-1-phosphate.

Figure 16: Capillary electrophoresis results of FITC-derivitized 2CFE 3 polypeptide with and without D-glucosamine-6-phosphate (substrate) to produce the product D-glucosamine-1-phosphate, using laser-induced fluorescence, as described in Example 13, *infra*. Electropherogram of D-glucosamine-6-phosphate (putative substrate), 2CFE 3 reacted with D-glucosamine-6-phosphate, and the product glucosamine-1-phosphate.

Figure 17: Gel electrophoresis of 2CFE 86 eluted from an Ni-NTA column, as described in Example 13, *infra*.

Figure 18: HPLC analysis of a coupled reaction including 2CFE 3, 2CFE 86, and D-glucosamine-6-phosphate to produce the product, UDP-N-acetylglucosamine-1-phosphate (UDPAG), as described in Example 13, *infra*.

Figure 19: A fatty acid biosynthesis pathway.

Figure 20: Size exclusion chromatography to determine the molecular weight and oligomeric form of 2CFE 34, as described in Example 14, *infra*. Selected eluted samples were sized by gel electrophoresis.

- 5 Figure 21: Gel electrophoresis of 2CFE 41 eluted from a Ni-NTA column, as described in Example 15, *infra*.

Figure 22: Capillary electrophoresis results of 2CFE 40, 41, and 46, as described in Example 15, *infra*.

10

Figure 23: Depicts a schematic diagram of a ligand which binds 2CFE 34. The ligand is 2-phenyl-N-(3 carboxyl-4hydroxyphenyl) azabicyclo [4.3.0] nona-2, 8-diene.

- Figure 24: Depicts a schematic diagram of a ligand which binds 2CFE 43. The ligand is N-(3, 5-dinitrobenzyl)-7-trifluoromethyl benza diaza furanolactone.
- 15

Figure 25: Depicts a schematic diagram of a ligand which binds 2CFE 43. The ligand is 2-amino (N-para-methylphenyl sulfonamide)-3-phenylpropionic acid.

- 20 Figure 26: A nucleic acid sequence of 2CFE1 deposited with the American Type Culture Collection as ATCC designation \_\_\_\_\_ on December 20, 2000.

Figure 27: A nucleic acid sequence of 2CFE2 deposited with the American Type Culture Collection as ATCC designation \_\_\_\_\_ on December 20, 2000.

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Figure 28: A nucleic acid sequence of 2CFE3 deposited with the American Type Culture Collection as ATCC designation \_\_\_\_\_ on December 20, 2000.

- Figure 29: A nucleic acid sequence of 2CFE4 deposited with the American Type Culture Collection as ATCC designation \_\_\_\_\_ on December 20, 2000.
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Figure 30: A nucleic acid sequence of 2CFE5 deposited with the American Type Culture Collection as ATCC designation \_\_\_\_\_ on December 20, 2000.

- 5 Figure 31: A nucleic acid sequence of 2CFE6 deposited with the American Type Culture Collection as ATCC designation \_\_\_\_\_ on December 20, 2000.

Figure 32: A nucleic acid sequence of 2CFE7 deposited with the American Type Culture Collection as ATCC designation \_\_\_\_\_ on December 20, 2000.

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Figure 33: A nucleic acid sequence of 2CFE8 deposited with the American Type Culture Collection as ATCC designation \_\_\_\_\_ on December 20, 2000.

- 15 Figure 34: A nucleic acid sequence of 2CFE9 deposited with the American Type Culture Collection as ATCC designation \_\_\_\_\_ on December 20, 2000.

Figure 35: A nucleic acid sequence of 2CFE10 deposited with the American Type Culture Collection as ATCC designation \_\_\_\_\_ on December 20, 2000.

- 20 Figure 36: A nucleic acid sequence of 2CFE11 deposited with the American Type Culture Collection as ATCC designation \_\_\_\_\_ on December 20, 2000.

Figure 37: A nucleic acid sequence of 2CFE12 deposited with the American Type Culture Collection as ATCC designation \_\_\_\_\_ on December 20, 2000.

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Figure 38: A nucleic acid sequence of 2CFE13 deposited with the American Type Culture Collection as ATCC designation \_\_\_\_\_ on December 20, 2000.

- 30 Figure 39: A nucleic acid sequence of 2CFE14 deposited with the American Type Culture Collection as ATCC designation \_\_\_\_\_ on December 20, 2000.



Figure 40: A nucleic acid sequence of 2CFE15 deposited with the American Type Culture Collection as ATCC designation \_\_\_\_\_ on December 20, 2000.

5 Figure 41: A nucleic acid sequence of 2CFE16 deposited with the American Type Culture Collection as ATCC designation \_\_\_\_\_ on December 20, 2000.

Figure 42: A nucleic acid sequence of 2CFE17 deposited with the American Type Culture Collection as ATCC designation \_\_\_\_\_ on December 20, 2000.

10 Figure 43: A nucleic acid sequence of 2CFE19 deposited with the American Type Culture Collection as ATCC designation \_\_\_\_\_ on December 20, 2000.

15 Figure 44: A nucleic acid sequence of 2CFE21 deposited with the American Type Culture Collection as ATCC designation \_\_\_\_\_ on December 20, 2000.

Figure 45: A nucleic acid sequence of 2CFE24 deposited with the American Type Culture Collection as ATCC designation \_\_\_\_\_ on December 20, 2000.

20 Figure 46: A nucleic acid sequence of 2CFE25 deposited with the American Type Culture Collection as ATCC designation \_\_\_\_\_ on December 20, 2000.

Figure 47: A nucleic acid sequence of 2CFE26 deposited with the American Type Culture Collection as ATCC designation \_\_\_\_\_ on December 20, 2000.

25 Figure 48: A nucleic acid sequence of 2CFE27 deposited with the American Type Culture Collection as ATCC designation \_\_\_\_\_ on December 20, 2000.

30 Figure 49: A nucleic acid sequence of 2CFE28 deposited with the American Type Culture Collection as ATCC designation \_\_\_\_\_ on December 20, 2000.

Figure 50: A nucleic acid sequence of 2CFE29 deposited with the American Type Culture Collection as ATCC designation \_\_\_\_\_ on December 20, 2000.

5 Figure 51: A nucleic acid sequence of 2CFE30 deposited with the American Type Culture Collection as ATCC designation \_\_\_\_\_ on December 20, 2000.

Figure 52: A nucleic acid sequence of 2CFE31 deposited with the American Type Culture Collection as ATCC designation \_\_\_\_\_ on December 20, 2000.

10 Figure 53: A nucleic acid sequence of 2CFE32 deposited with the American Type Culture Collection as ATCC designation \_\_\_\_\_ on December 20, 2000.

Figure 54: A nucleic acid sequence of 2CFE33 deposited with the American Type Culture Collection as ATCC designation \_\_\_\_\_ on December 20, 2000.

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Figure 55: A nucleic acid sequence of 2CFE34 deposited with the American Type Culture Collection as ATCC designation \_\_\_\_\_ on December 20, 2000.

Figure 56: A nucleic acid sequence of 2CFE35 deposited with the American Type Culture Collection as ATCC designation \_\_\_\_\_ on December 20, 2000.

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Figure 57: A nucleic acid sequence of 2CFE36 deposited with the American Type Culture Collection as ATCC designation \_\_\_\_\_ on December 20, 2000.

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Figure 59: A nucleic acid sequence of 2CFE38 deposited with the American Type Culture Collection as ATCC designation \_\_\_\_\_ on December 20, 2000.

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Figure 60: A nucleic acid sequence of 2CFE39 deposited with the American Type Culture Collection as ATCC designation \_\_\_\_\_ on December 20, 2000.

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Figure 62: A nucleic acid sequence of 2CFE41 deposited with the American Type Culture Collection as ATCC designation \_\_\_\_\_ on December 20, 2000.

10 Figure 63: A nucleic acid sequence of 2CFE42 deposited with the American Type Culture Collection as ATCC designation \_\_\_\_\_ on December 20, 2000.

15 Figure 64: A nucleic acid sequence of 2CFE43 deposited with the American Type Culture Collection as ATCC designation \_\_\_\_\_ on December 20, 2000.

Figure 65: A nucleic acid sequence of 2CFE44 deposited with the American Type Culture Collection as ATCC designation \_\_\_\_\_ on December 20, 2000.

20 Figure 66: A nucleic acid sequence of 2CFE45 deposited with the American Type Culture Collection as ATCC designation \_\_\_\_\_ on December 20, 2000.

Figure 67: A nucleic acid sequence of 2CFE46 deposited with the American Type Culture Collection as ATCC designation \_\_\_\_\_ on December 20, 2000.

25 Figure 68: A nucleic acid sequence of 2CFE47 deposited with the American Type Culture Collection as ATCC designation \_\_\_\_\_ on December 20, 2000.

30 Figure 69: A nucleic acid sequence of 2CFE48 deposited with the American Type Culture Collection as ATCC designation \_\_\_\_\_ on December 20, 2000.

Figure 70: A nucleic acid sequence of 2CFE49 deposited with the American Type Culture Collection as ATCC designation \_\_\_\_\_ on December 20, 2000.

5 Figure 71: A nucleic acid sequence of 2CFE50 deposited with the American Type Culture Collection as ATCC designation \_\_\_\_\_ on December 20, 2000.

Figure 72: A nucleic acid sequence of 2CFE51 deposited with the American Type Culture Collection as ATCC designation \_\_\_\_\_ on December 20, 2000.

10 Figure 73: A nucleic acid sequence of 2CFE52 deposited with the American Type Culture Collection as ATCC designation \_\_\_\_\_ on December 20, 2000.

Figure 74: A nucleic acid sequence of 2CFE53 deposited with the American Type Culture Collection as ATCC designation \_\_\_\_\_ on December 20, 2000.

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Figure 75: A nucleic acid sequence of 2CFE54 deposited with the American Type Culture Collection as ATCC designation \_\_\_\_\_ on December 20, 2000.

20 Figure 76: A nucleic acid sequence of 2CFE55 deposited with the American Type Culture Collection as ATCC designation \_\_\_\_\_ on December 20, 2000.

Figure 77: A nucleic acid sequence of 2CFE56 deposited with the American Type Culture Collection as ATCC designation \_\_\_\_\_ on December 20, 2000.

25 Figure 78: A nucleic acid sequence of 2CFE57 deposited with the American Type Culture Collection as ATCC designation \_\_\_\_\_ on December 20, 2000.

Figure 79: A nucleic acid sequence of 2CFE58 deposited with the American Type Culture Collection as ATCC designation \_\_\_\_\_ on December 20, 2000.

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Figure 80: A nucleic acid sequence of 2CFE59 deposited with the American Type Culture Collection as ATCC designation \_\_\_\_\_ on December 20, 2000.

5 Figure 81: A nucleic acid sequence of 2CFE60 deposited with the American Type Culture Collection as ATCC designation \_\_\_\_\_ on December 20, 2000.

Figure 82: A nucleic acid sequence of 2CFE61 deposited with the American Type Culture Collection as ATCC designation \_\_\_\_\_ on December 20, 2000.

10 Figure 83: A nucleic acid sequence of 2CFE62 deposited with the American Type Culture Collection as ATCC designation \_\_\_\_\_ on December 20, 2000.

Figure 84: A nucleic acid sequence of 2CFE64 deposited with the American Type Culture Collection as ATCC designation \_\_\_\_\_ on December 20, 2000.

15 Figure 85: A nucleic acid sequence of 2CFE65 deposited with the American Type Culture Collection as ATCC designation \_\_\_\_\_ on December 20, 2000.

Figure 86: A nucleic acid sequence of 2CFE66 deposited with the American Type Culture Collection as ATCC designation \_\_\_\_\_ on December 20, 2000.

20 Figure 87: A nucleic acid sequence of 2CFE67 deposited with the American Type Culture Collection as ATCC designation \_\_\_\_\_ on December 20, 2000.

25 Figure 88: A nucleic acid sequence of 2CFE68 deposited with the American Type Culture Collection as ATCC designation \_\_\_\_\_ on December 20, 2000.

Figure 89: A nucleic acid sequence of 2CFE69 deposited with the American Type Culture Collection as ATCC designation \_\_\_\_\_ on December 20, 2000.

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Figure 90: A nucleic acid sequence of 2CFE70 deposited with the American Type Culture Collection as ATCC designation \_\_\_\_\_ on December 20, 2000.

5 Figure 91: A nucleic acid sequence of 2CFE71 deposited with the American Type Culture Collection as ATCC designation \_\_\_\_\_ on December 20, 2000.

Figure 92: A nucleic acid sequence of 2CFE72 deposited with the American Type Culture Collection as ATCC designation \_\_\_\_\_ on December 20, 2000.

10 Figure 93: A nucleic acid sequence of 2CFE75 deposited with the American Type Culture Collection as ATCC designation \_\_\_\_\_ on December 20, 2000.

Figure 94: A nucleic acid sequence of 2CFE76 deposited with the American Type Culture Collection as ATCC designation \_\_\_\_\_ on December 20, 2000.

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Figure 95: A nucleic acid sequence of 2CFE78 deposited with the American Type Culture Collection as ATCC designation \_\_\_\_\_ on December 20, 2000.

20 Figure 96: A nucleic acid sequence of 2CFE79 deposited with the American Type Culture Collection as ATCC designation \_\_\_\_\_ on December 20, 2000.

Figure 97: A nucleic acid sequence of 2CFE80 deposited with the American Type Culture Collection as ATCC designation \_\_\_\_\_ on December 20, 2000.

25 Figure 98: A nucleic acid sequence of 2CFE81 deposited with the American Type Culture Collection as ATCC designation \_\_\_\_\_ on December 20, 2000.

Figure 99: A nucleic acid sequence of 2CFE82 deposited with the American Type Culture Collection as ATCC designation \_\_\_\_\_ on December 20, 2000.

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Figure 100: A nucleic acid sequence of 2CFE83 deposited with the American Type Culture Collection as ATCC designation \_\_\_\_\_ on December 20, 2000.

5 Figure 101: A nucleic acid sequence of 2CFE84 deposited with the American Type Culture Collection as ATCC designation \_\_\_\_\_ on December 20, 2000.

Figure 102: A nucleic acid sequence of 2CFE85 deposited with the American Type Culture Collection as ATCC designation \_\_\_\_\_ on December 20, 2000.

10 Figure 103: A nucleic acid sequence of 2CFE86 deposited with the American Type Culture Collection as ATCC designation \_\_\_\_\_ on December 20, 2000.

Figure 104: A nucleic acid sequence of 2CFE87 deposited with the American Type Culture Collection as ATCC designation \_\_\_\_\_ on December 20, 2000.

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Figure 105: A nucleic acid sequence of 2CFE88 deposited with the American Type Culture Collection as ATCC designation \_\_\_\_\_ on December 20, 2000.

20 Figure 106: A nucleic acid sequence of 2CFE89 deposited with the American Type Culture Collection as ATCC designation \_\_\_\_\_ on December 20, 2000.

Figure 107: A nucleic acid sequence of 2CFE90 deposited with the American Type Culture Collection as ATCC designation \_\_\_\_\_ on December 20, 2000.

25 Figure 108: A nucleic acid sequence of 2CFE91 deposited with the American Type Culture Collection as ATCC designation \_\_\_\_\_ on December 20, 2000.

Figure 109: A nucleic acid sequence of 2CFE92 deposited with the American Type Culture Collection as ATCC designation \_\_\_\_\_ on December 20, 2000.

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Figure 110: A nucleic acid sequence of 2CFE94 deposited with the American Type Culture Collection as ATCC designation \_\_\_\_\_ on December 20, 2000.

5 Figure 111: A nucleic acid sequence of 2CFE95 deposited with the American Type Culture Collection as ATCC designation \_\_\_\_\_ on December 20, 2000.

Figure 112: A nucleic acid sequence of 2CFE96 deposited with the American Type Culture Collection as ATCC designation \_\_\_\_\_ on December 20, 2000.

10 Figure 113: A nucleic acid sequence of 2CFE97 deposited with the American Type Culture Collection as ATCC designation \_\_\_\_\_ on December 20, 2000.

Figure 114: A nucleic acid sequence of 2CFE99 deposited with the American Type Culture Collection as ATCC designation \_\_\_\_\_ on December 20, 2000.

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Figure 115: A nucleic acid sequence of 2CFE101 deposited with the American Type Culture Collection as ATCC designation \_\_\_\_\_ on December 20, 2000.

20 Figure 116: A nucleic acid sequence of 2CFE102 deposited with the American Type Culture Collection as ATCC designation \_\_\_\_\_ on December 20, 2000.

Figure 117: A nucleic acid sequence of 2CFE103 deposited with the American Type Culture Collection as ATCC designation \_\_\_\_\_ on December 20, 2000.

25 Figure 118: A nucleic acid sequence of 2CFE104 deposited with the American Type Culture Collection as ATCC designation \_\_\_\_\_ on December 20, 2000.

Figure 119: A nucleic acid sequence of 2CFE105 deposited with the American Type Culture Collection as ATCC designation \_\_\_\_\_ on December 20, 2000.

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Figure 120: A nucleic acid sequence of 2CFE106 deposited with the American Type Culture Collection as ATCC designation \_\_\_\_\_ on December 20, 2000.

5 Figure 121: A nucleic acid sequence of 2CFE107 deposited with the American Type Culture Collection as ATCC designation \_\_\_\_\_ on December 20, 2000.

Figure 122: A nucleic acid sequence of 2CFE108 deposited with the American Type Culture Collection as ATCC designation \_\_\_\_\_ on December 20, 2000.

10 Figure 123: A nucleic acid sequence of 2CFE109 deposited with the American Type Culture Collection as ATCC designation \_\_\_\_\_ on December 20, 2000.

Figure 124: A nucleic acid sequence of 2CFE111 deposited with the American Type Culture Collection as ATCC designation \_\_\_\_\_ on December 20, 2000.

15 Figure 125: A nucleic acid sequence of 2CFE112 deposited with the American Type Culture Collection as ATCC designation \_\_\_\_\_ on December 20, 2000.

Figure 126: A nucleic acid sequence of 2CFE113 deposited with the American Type Culture Collection as ATCC designation \_\_\_\_\_ on December 20, 2000.

20 Figure 127: A nucleic acid sequence of 2CFE114 deposited with the American Type Culture Collection as ATCC designation \_\_\_\_\_ on December 20, 2000.

25 Figure 128: A nucleic acid sequence of 2CFE115 deposited with the American Type Culture Collection as ATCC designation \_\_\_\_\_ on December 20, 2000.

Figure 129: A nucleic acid sequence of 2CFE116 deposited with the American Type Culture Collection as ATCC designation \_\_\_\_\_ on December 20, 2000.

30

Figure 130: A nucleic acid sequence of 2CFE117 deposited with the American Type Culture Collection as ATCC designation \_\_\_\_\_ on December 20, 2000.

Figure 131: Schematic structures of alkylolids which are ligands, for example, of 2CFE42.

5

## DETAILED DESCRIPTION OF THE INVENTION

### Definitions

10 All scientific and technical terms used in this application have meanings commonly used in the art unless otherwise specified. As used in this application, the following words or phrases have the meanings specified.

As used herein, a *ceg* nucleic acid molecule is said to be "isolated" when the nucleic acid  
15 molecule is substantially separated from contaminant nucleic acid molecules that encode polypeptides other than CEGs. Additionally, isolated nucleic acid molecule refers to any RNA or DNA sequence obtained from a natural source, or constructed by recombinant methods, or synthesized. A skilled artisan can readily employ nucleic acid isolation procedures to obtain an isolated nucleic acid molecule having *ceg* sequences.

20

The term "*ceg*" includes all isolated forms of *ceg* nucleotide and CEG amino acid sequences disclosed herein. The *ceg* sequences encode gene products that have essential biological functions in bacterial cells, such as, for example, nucleotide biosynthesis, amino acid biosynthesis, DNA replication, RNA transcription, protein translation, DNA  
25 recombination, DNA repair, biosynthesis of cofactors (e.g., Coenzyme A), biosynthesis of prosthetic groups, cellular processes (e.g., chaperones, cell division, and polypeptide secretion), energy metabolism (e.g., pentose phosphate pathway, glycolysis, gluconeogenesis), fatty acid biosynthesis, cell wall biosynthesis, and/or biosynthesis of purines, pyrimidines, nucleosides, and nucleotides. Accordingly, the gene products of the  
30 *ceg* nucleotide sequences are required for viability of bacterial cells. The term "*ceg*" also includes variants having nucleotide sequence similarity to the disclosed *ceg* sequences,

including sequences isolated from various bacterial genera and species, allelic variants, mutant variants, and *ceg* variants that encode conservative and non-conservative amino acid substitutions. The present invention also provides for all *ceg* sequences generated by recombinant DNA technology, including complementary sequences, *ceg* sequences that  
5 hybridize to the sequences of the invention at high stringency hybridization conditions, fusion genes comprising a *ceg* sequence, and codon usage variants.

The term "essential genes" refers to a nucleotide sequence that encodes a gene product having a function which is required for cell viability. The term "essential protein" refers  
10 to a polypeptide that is encoded by an essential gene and has a function that is required for cell viability. Accordingly, a mutation that disrupts the function of the essential gene or essential proteins results in a loss of viability of cells harboring the mutation.

"Non-essential genes" or "non-essential proteins" refer to genomic information or the  
15 protein(s) or RNAs encoded therefrom which, when disrupted by a mutation, do not result in a loss of viability of cells harboring said mutation under defined laboratory conditions.

As used herein, a nucleotide sequence is said to be "identical" to another reference  
20 sequence when both nucleotide sequences are exactly alike.

As used herein, a nucleotide sequence is said to be "similar" to another reference sequence when a comparison of the two sequences shows that they have a low level of sequence differences. For example, two sequences are considered to be similar to each  
25 other when the percentage of nucleotides that are shared between the two sequences is between about 70 % to 99.99% over the entire length of the two sequences.

As used herein an amino acid sequence is said to be "similar" to another reference sequence when a comparison of the two sequences shows that they have a low level of  
30 sequence differences. For example, two sequences are considered to be similar to each

other when the percentage of amino acids that are shared between the two sequences may be between about 30% to 100% identity over the entire length of the two sequences.

5 As used herein, an "allele" or "allelic sequence" is an alternative form of the naturally-occurring *ceg* sequence. Alleles result from a mutation, that changes the nucleotide sequence, and generally produce altered mRNAs or polypeptides whose structure or function may or may not be altered.

10 "Substantially purified" as used herein means a specific isolated nucleic acid or protein, or fragment thereof, in which substantially all contaminants (i.e. substances that differ from said specific molecule) have been separated from said nucleic acid or protein.

15 In a host cell, an "endogenous" sequence as used herein means a nucleic acid sequence that is naturally-occurring and resides within the host genome.

In a host cell, an "exogenous" sequence as used herein means an isolated nucleic acid sequence that is introduced into the host cell, using any one of a variety of introduction methods, such as transfection, electroporation, cationic lipid or salt treatment methods.

20 "Knockout mutant" or "knockout mutation" as used herein refers to an *in vitro* engineered disruption of a region of endogenous chromosomal DNA (e.g., disruption of the genome), typically within a protein coding region. A knockout mutation can be generated by inserting an exogenous DNA sequence into the homologous endogenous sequence. A knockout mutation occurring in a protein coding region is expected to disrupt normal  
25 expression of the protein coding region. This usually leads to loss of the function provided by the protein.

30 In order that the invention herein described may be more fully understood, the following description is set forth.

## A) MOLECULES OF THE INVENTION

### 1.) CEG NUCLEIC ACID MOLECULES

- 5 The present invention provides isolated and recombinant *ceg* nucleic acid molecules and fragments thereof, and related molecules, such as sequences complementary to *ceg* sequences or a portion thereof, and those that hybridize to the nucleic acid molecules of the invention.
- 10 The *ceg* polynucleotide sequences, also referred to herein as nucleic acid molecules of the invention, are preferably in isolated form, including DNA, RNA, DNA/RNA hybrids, and related molecules, and fragments thereof. Specifically contemplated are genomic DNA, ribozymes, and antisense molecules, as well as nucleic acid molecules based on an alternative backbone or including alternative bases, whether derived from natural sources or
- 15 synthesized. Embodiments of particular *ceg* polynucleotide and amino acid sequences include, but are not limited to, the sequences described in Tables I and II (e.g., SEQ ID NOS:1-113, 114-226 and SEQ ID NOS: 227-339, 340-452, respectively). The *ceg* polynucleotide and amino acid sequences were designated *cef* which stands for CEG For Expression.
- 20 Biological samples of the 2CFE nucleic acid molecules (e.g., SEQ ID NOS: 227-331) were deposited on December 20, 2000 with the American Type Culture Collection (ATCC), 10801 University Blvd., Manassas, VA 20110-2209.

TABLE I

CFE Designation	SEQ. ID NO. (Nucleotide)	SEQ. ID NO. (Polypeptide)	POLARITY
CFE 1	1	114	+
CFE 2	2	115	-
CFE 3	3	116	-
CFE 4	4	117	+
CFE 5	5	118	-
CFE 6	6	119	+

TABLE I

CFE Designation	SEQ. ID NO. (Nucleotide)	SEQ. ID NO. (Polypeptide)	POLARITY
CFE 7	7	120	-
CFE 8	8	121	+
CFE 9	9	122	+
CFE 10	10	123	+
CFE 11	11	124	+
CFE 12	12	125	+
CFE 13	13	126	-
CFE 14	14	127	+
CFE 15	15	128	-
CFE 16	16	129	-
CFE 17	17	130	-
CFE 19	18	131	+
CFE 21	19	132	-
CFE 24	20	133	-
CFE 25	21	134	+
CFE 26	22	135	-
CFE 27	23	136	+
CFE 28	24	137	-
CFE 29	25	138	-
CFE 30	26	139	-
CFE 31	27	140	+
CFE 32	28	141	+
CFE 33	29	142	-
CFE 34	30	143	+
CFE 35	31	144	+
CFE 36	32	145	+
CFE 37	33	146	-
CFE 38	34	147	+
CFE 39	35	148	-
CFE 40	36	149	-
CFE 41	37	150	-
CFE 42	38	151	-
CFE 43	39	152	-
CFE 44	40	153	+
CFE 45	41	154	-
CFE 46	42	155	-

TABLE I

CFE Designation	SEQ. ID NO. (Nucleotide)	SEQ. ID NO. (Polypeptide)	POLARITY
CFE 47	43	156	-
CFE 48	44	157	
CFE 49	45	158	+
CFE 50	46	159	+
CFE 51	47	160	+
CFE 52	48	161	-
CFE 53	49	162	+
CFE 54	50	163	+
CFE 55	51	164	+
CFE 56	52	165	+
CFE 57	53	166	+
CFE 58	54	167	+
CFE 59	55	168	-
CFE 60	56	169	+
CFE 61	57	170	+
CFE 62	58	171	
CFE 63	59	172	
CFE 64	60	173	+
CFE 65	61	174	+
CFE 66	62	175	+
CFE 67	63	176	+
CFE 68	64	177	-
CFE 69	65	178	+
CFE 70	66	179	+
CFE 71	67	180	-
CFE 72	68	181	-
CFE 73	69	182	+
CFE 74	70	183	-
CFE 75	71	184	-
CFE 76	72	185	+
CFE 77	73	186	
CFE 78	74	187	+
CFE 79	75	188	-
CFE 80	76	189	-
CFE 81	77	190	+
CFE 82	78	191	

TABLE I

CFE Designation	SEQ. ID NO. (Nucleotide)	SEQ. ID NO. (Polypeptide)	POLARITY
CFE 83	79	192	-
CFE 84	80	193	-
CFE 85	81	194	-
CFE 86	82	195	-
CFE 87	83	196	-
CFE 88	84	197	-
CFE 89	85	198	+
CFE 90	86	199	+
CFE 91	87	200	-
CFE 92	88	201	-
CFE 93	89	202	+
CFE 94	90	203	+
CFE 95	91	204	+
CFE 96	92	205	+
CFE 97	93	206	-
CFE 98	94	207	-
CFE 99	95	208	+
CFE 100	96	209	-
CFE 101	97	210	-
CFE 102	98	211	+
CFE 103	99	212	-
CFE 104	100	213	+
CFE 105	101	214	-
CFE 106	102	215	-
CFE 107	103	216	-
CFE 108	104	217	+
CFE 109	105	218	-
CFE110	106	219	-
CFE 111	107	220	-
CFE 112	108	221	-
CFE 113	109	222	-
CFE 114	110	223	-
CFE 115	111	224	-
CFE 116	112	225	-
CFE 117	113	226	-



TABLE II

CFE Designation	SEQ. ID NO. (Nucleotide)	SEQ. ID NO. (Polypeptide)	FIGURE
2CFE 1			26
2CFE 2			27
2CFE 3			28
2CFE 4			29
2CFE 5			30
2CFE 6			31
2CFE 7			32
2CFE 8			33
2CFE 9			34
2CFE 10			35
2CFE 11			36
2CFE 12			37
2CFE 13			38
2CFE 14			39
2CFE 15			40
2CFE 16			41
2CFE 17			42
2CFE 19			43
2CFE 21			44
2CFE 24			45
2CFE 25			46
2CFE 26			47
2CFE 27			48
2CFE 28			49
2CFE 29			50
2CFE 30			51
2CFE 31			52
2CFE 32			53
2CFE 33			54
2CFE 34			55
2CFE 35			56
2CFE 36			57
2CFE 37			58
2CFE 38			59
2CFE 39			60

CFE Designation	SEQ. ID NO. (Nucleotide)	SEQ. ID NO. (Polypeptide)	FIGURE
2CFE 40			61
2CFE 41			62
2CFE 42			63
2CFE 43			64
2CFE 44			65
2CFE 45			66
2CFE 46			67
2CFE 47			68
2CFE 48			69
2CFE 49			70
2CFE 50			71
2CFE 51			72
2CFE 52			73
2CFE 53			74
2CFE 54			75
2CFE 55			76
2CFE 56			77
2CFE 57			78
2CFE 58			79
2CFE 59			80
2CFE 60			81
2CFE 61			82
2CFE 62			83
2CFE 64			84
2CFE 65			85
2CFE 66			86
2CFE 67			87
2CFE 68			88
2CFE 69			89
2CFE 70			90
2CFE 71			91
2CFE 72			92
2CFE 75			93
2CFE 76			94
2CFE 78			95
2CFE 79			96
2CFE 80			97

CFE Designation	SEQ. ID NO. (Nucleotide)	SEQ. ID NO. (Polypeptide)	FIGURE
2CFE 81			98
2CFE 82			99
2CFE 83			100
2CFE 84			101
2CFE 85			102
2CFE 86			103
2CFE 87			104
2CFE 88			105
2CFE 89			106
2CFE 90			107
2CFE 91			108
2CFE 92			109
2CFE 94			110
2CFE 95			111
2CFE 96			112
2CFE 97			113
2CFE 99			114
2CFE 101			115
2CFE 102			116
2CFE 103			117
2CFE 104			118
2CFE 105			119
2CFE 106			120
2CFE 107			121
2CFE 108			122
2CFE 109			123
2CFE 111			124
2CFE 112			125
2CFE 113			126
2CFE 114			127
2CFE 115			128
2CFE 116			129
2CFE 117			130

a) Variant *ceg* Nucleotide Sequences

5 The present invention also provides nucleic acid molecules having a nucleotide sequence substantially identical or similar to the *ceg* sequences (SEQ ID NOS: 1-113, 227-331) disclosed herein.

10 The present invention provides nucleotide sequences which are similar to SEQ ID NOS:1-113 and/or SEQ ID NOS:227-331. The present invention provides nucleotide sequences which vary from SEQ ID NOS:1-113 or 227-331 by a range of about 1% to about 70%.

15 The present invention encompasses variations in polynucleotide sequences resulting from mutations and/or from transfer of genetic material from one cell to another (e.g., horizontal gene transfer or horizontal gene exchange).

20 The present invention also provides for variants of the polynucleotide *ceg* sequences disclosed herein, including variants isolated from naturally-occurring sources, those generated by recombinant DNA technology or other in vitro synthesis methodologies (e.g., PCR). The variant polynucleotide sequences of the invention encode polypeptides that exhibit the biological activity of naturally-occurring CEG polypeptides, such as activity required for bacterial cell viability.

25 In general, for example, a variant of *ceg* polynucleotide sequences may encode a polypeptide that differs by one or more amino acid substitutions. The variant may have conservative changes, wherein a substituted amino acid has similar structural or chemical properties, eg, replacement of leucine with isoleucine.

30 A polynucleotide sequence can encode conservative amino acid substitutions without altering either the conformation or the function of the polypeptide. Such changes include substituting any of isoleucine (I), valine (V), and leucine (L) for any other of these

hydrophobic amino acids; aspartic acid (D) for glutamic acid (E) and vice versa; glutamine (Q) for asparagine (N) and vice versa; and serine (S) for threonine (T) and vice versa. Other substitutions can also be considered conservative, depending on the environment of the particular amino acid and its role in the three-dimensional structure of the protein. For example, glycine (G) and alanine (A) can frequently be interchangeable, as can alanine (A) and valine (V). Methionine (M), which is relatively hydrophobic, can frequently be interchanged with leucine and isoleucine, and sometimes with valine. Lysine (K) and arginine (R) are frequently interchangeable in locations in which the significant feature of the amino acid residue is its charge and the differing pK's of these two amino acid residues are not significant. Still other changes can be considered "conservative" in particular environments.

A variant may also have nonconservative changes, eg, replacement of a glycine with a tryptophan. Other variations may also include amino acid deletions or insertions, or both. Guidance in determining which and how many amino acid residues may be substituted, inserted or deleted without abolishing biological or immunological activity may be found using computer programs well known in the art, for example, DNASTAR software.

Another type of *ceg* sequence variant includes naturally-occurring allelic variants of *ceg* which share significant similarity (e.g., between about 30- 99%) to the disclosed CEG polypeptide sequence. Allelic variants of the *ceg* sequences can encode conservative or non-conservative amino acid substitutions of the CEG polypeptide sequence herein described.

An example of allelic variants of *ceg* are mutant alleles of *ceg* polynucleotide sequences that encode a polypeptide having one or more changes in the polypeptide sequence, such as amino acid substitutions, deletions, insertions, frame shifts, or truncations. The mutant alleles of *ceg* may or may not encode a CEG polypeptide having the same biological functions as wild-type CEG proteins.

Variations in the bacterial genomic sequences can also arise from transfer of genetic material to another bacterial cell. The transfer of gene sequences can occur intraspecies or interspecies. Gene transfer can occur between bacterial cells which are members of the same or different populations. A population includes, but is not limited to, a serotype isolate, a clinical isolate, a naturally-occurring isolate, a strain, and a species. The transfer of genetic material can occur between cells within a population; for example transfer between serotype A to serotype A, or between *S. pneumoniae* and *S. pneumoniae*. The transfer of genetic material can occur between cells of different populations; for example, between serotype A to serotype B or *S. pneumoniae* and *S. mutans*.

Gene transfer can give rise to mutant or polymorphic variant genes sequences. In rare cases, gene transfer introduces new gene sequences that confer a new phenotype, such as antibiotic resistance. The transfer of genetic material includes transfer of large regions of genomic sequences which include partial gene sequences, whole single gene sequences, or multiple gene sequences. This mode of transfer can give rise to replacement of native whole gene sequences or introduction of new sequences in the recipient cell. This mode of transfer gives rise to mosaic gene sequences in the recipient cell.

The variation of genomic sequences resulting from gene transfer can be examined using molecular techniques, including: multilocus enzyme electrophoresis (Selander, R. K., et al., 1986 *Appl. Environ. Microbiol.* 51:837-884); and restriction endonuclease cleavage electrophoretic profiling (Coffey, T. J., et al., 1991 *Mol. Microbio.* 5:2255-2260); pulse-field gel electrophoresis fingerprinting (Bygraves, J. A. and Maiden, M. C. J. 1992 *J. Gen. Microbiol.* 138:523-531); and ribotyping (Stull, T. L., et al., 1988 *J. Infect. Dis.* 157:280-286). The degree of variation can vary greatly, and ranges from little or no variation as exemplified by gene sequences of *E. coli* (Caugant, d. A., et al., 1981 *Genetics* 98:467-490; Whittam, T. S., et al., 1983 *Mol. Biol. Evol.* 1:67-83; Souza, V., et al., 1992 *Proc. Natl. Acad. Sci. USA* 89:8389-8393) and *Salmonella* (Selander, R. K., et al., 1990 *Infect. Immun.* 58:2262-2275; Selander, R.K. and Smith, N. H. 1990 *Rev. Med. Microbiol.* 1:219-228; Smith, J. M., et al., 1993 *Proc. Natl. Acad. Sci. USA* 90:4384-

4388), to extensive gene transfer in *Neisseria gonorrhoeae* (Smith, J. M., et al., 1993 *Proc. Natl. Acad. Sci. USA* 90:4384-4388).

Gene transfer can be examined between various isolates of a particular microbial species which are antibiotic-sensitive or antibiotic-resistant (Coffey, T. J., et al., 1991 *Molec. Microbiol.* 5:2255-2260). Molecular biology techniques can be utilized to study the degree of transfer between populations, such as, for example, the degree of gene transfer between serotypes, isolates, strains, or species. The degree of transfer can be examined by comparing, for example, the penicillin binding proteins and numerous different loci which encode metabolic enzymes or capsular biosynthesis enzymes.

For example, intra-species, inter-serotype, gene transfer is possible (Coffey, T. J., et al., 1991 *supra*). Additionally, intraspecies gene transfer in *S. pneumoniae* (Coffey, T. J., et al., 1998 *Mol. Microbiol.* 27:73-83), *Vibrio cholerae* (Bik, E. M., et al., 1995 *EMBO J.* 14:209-216), and *Haemophilus influenzae* (Kroll, J. S. and Moxon, E. R. 1990 *J. Bacteriol.* 172: 1374-1379) are possible.

Interspecies gene transfer is also possible (Dowson, C. G., et al., 1989 *Proc. Natl. Acad. Sci. USA* 86:8842-8846; Laibl, G., et al., 1991 *Mol. Microbiol.* 5:1993-2002; Bourgoin, F., et al., 1999 *Gene* 233:151-161).

Variant gene sequences arising from gene transfer can be continually generated in transformable bacteria (e.g., transformation competent), such as *S. pneumoniae*. For example, the worldwide spread of varying degrees of antibiotic resistance has been documented and reviewed (Dowson, C. G., et al., 1994 *Trends Microbiol.* 2:361-366; Spratt, B. G. in *Bacterial Cell Wall*, eds Ghuyssen J-M. and Hakenbeck, R. 1994 pp. 517-534; and reviewed in Maiden, M. C. J. 1998 *Clinic. Infect. Dis.* 27 (Supplement 1) S12-S20). For example, variant gene sequence arising from gene transfer can be tracked using a marker gene such as the gene which encodes the penicillin binding protein (Barcus, V. A., et al., 1995 *FEMS Microbiol. Lett.* 126:299-303). At the nucleotide level, gene sequences encoding the penicillin binding proteins in susceptible and resistant

strains differ by about 14% to 23% (Hakenbeck, R. 1995 *Biochem. Pharmacol.* 50:1121-1127; Spratt, B. G. in *Bacterial Cell Wall*, eds Ghuysen J-M. and Hakenbeck, R. 1994 pp. 517-534; Spratt, B. G., et al., 1991 *Neisseria meningitidis* and *Streptococcus pneumoniae* eds. Camisi, J., et al., pp. 73-83; Coffey, T. J., et al., 1995 *Micro. Drug Resist.* 1:29-34).

5

The *ceg* nucleotide sequences can be isolated from various species of *Streptococcus* including *Streptococcus pneumoniae*. Additionally, the *ceg* sequences can be isolated from other Streptococcal species, including *S. mutans*, *S. pyogenes*, and *S. thermophila*. The *ceg* polynucleotide sequences can also be isolated from strains of other bacterial genera including, but not limited to, *Streptococcus*, *Escherichia*, *Bacillus*, *Pseudomonas*, *Yersinia*, *Salmonella*, and *Haemophilus*.

10

The present invention additionally provides isolated codon-usage variants that differ from the disclosed *ceg* nucleotide sequences, yet do not alter the predicted CEG polypeptide sequence or function. The codon-usage variants may be generated by recombinant DNA technology. Codons may be selected to optimize the level of production of the *ceg* transcript or CEG polypeptide in a particular prokaryotic or eukaryotic expression host, in accordance with the frequency of codon utilized by the host cell. Alternative reasons for altering the nucleotide sequence encoding a CEG polypeptide include the production of RNA transcripts having more desirable properties, such as an extended half-life or increased stability. A multitude of variant *ceg* nucleotide sequences that encode the respective CEG polypeptide may be isolated, as a result of the degeneracy of the genetic code. Accordingly, the present invention contemplates selecting every possible triplet codon to generate every possible combination of nucleotide sequences that encode the disclosed CEG polypeptides. This particular embodiment provides isolated nucleotide sequences that vary from the sequences as described in SEQ ID NOs.: 1-113 or 227-331, such that each variant nucleotide sequence encodes a polypeptide having sequence identity with the amino acid sequences, as described in SEQ ID NOs.: 114-226 or 332-436, respectively.

20

25

30



### b) Complementary Sequences

The present invention includes polynucleotide sequences that are complementary to the sequences disclosed herein. The term "complementary" as used herein refers to the capacity of purine and/or pyrimidine nucleotides to associate through hydrogen bonding to form double stranded nucleic acid molecules. The following base pairs are related by complementarity: guanine and cytosine; adenine and thymine; and adenine and uracil. Complementary applies to all base pairs comprising at least two single-stranded nucleic acid molecules.

### c) Sequences Capable of Hybridizing

Another embodiment provides nucleic acid molecules that will hybridize to *ceg* sequences under hybridization conditions. It is readily apparent to one skilled in the art that the stringency of the hybridization condition selected will depend upon the characteristics of the nucleic acid molecule to be hybridized, such as, the length, the degree of complementarity (e.g., exact or non-exact complementarity), the percent A/T content, and the objective of the hybridization experiment.

The hybridization procedure may be performed in low stringency hybridization conditions. Low stringency hybridization conditions will permit hybridization between two nucleic acid molecules that differ from exact complementarity by about 25% to 70%. Hybridization under standard high stringency conditions will occur between two complementary nucleic acid molecules (e.g., 100% exact complementarity) or two complementary nucleic acid molecules that differ from exact complementarity by about 1% to about 70%.

The high stringency hybridization conditions that disfavor non-homologous base pairing are well known in the art. Typically, high stringency hybridization conditions, includes but is not limited to, hybridizing at 50 °C to 65 °C in 5X SSPE, and washing at 50 °C to

65 °C in 0.5X SSPE. Typically, low stringency conditions, includes but is not limited to, hybridizing at 35 °C to 37 °C in 5X SSPE and 40% to 45% formamide and washing at 42 °C in 1-2X SSPE. The conditions and formulas for high stringency hybridization methods are well known in the art and can be readily obtained in *Molecular Cloning: A Laboratory Manual* (2<sup>nd</sup> edition, Sambrook, Fritsch, and Maniatis 1989, Cold Spring Harbor Press) or in *Short Protocols in Molecular Biology* (Ausubel, F. M., et al., 1989, John Wiley & Sons).

#### d) Fragments of *ceg* Sequences

10

The invention further provides nucleic acid molecules having fragments of the *ceg* sequences, such as a portion of the *ceg* sequence (e.g., SEQ ID NOS:1-113, 227-331) disclosed herein. The size of the fragment will be determined by its intended use. For example, the length of the fragment to be used as a nucleic acid probe or PCR primer is  
15 chosen to obtain a relatively small number of false positives during probing or priming. Alternatively, a fragment of the *ceg* sequence may be used to construct a recombinant fusion gene having a *ceg* sequence fused to a non-*ceg* sequence.

The nucleic acid molecules, fragments thereof, and probes and primers of the present  
20 invention are useful for a variety of molecular biology techniques including, for example, hybridization screens of libraries, or detection and quantification of mRNA transcripts as a means for analysis of gene transcription and/or expression. Preferably, the probes and primers are DNA. A probe or primer length of at least 15 base pairs is suggested by theoretical and practical considerations (Wallace, B. and Miyada, G. 1987  
25 "Oligonucleotide Probes for the Screening of Recombinant DNA Libraries" in: *Methods in Enzymology*, 152:432-442, Academic Press). Other lengths of fragments, probes, or primers are possible and routine to determine.

The probes and primers of this invention can be prepared by methods well known to  
30 those skilled in the art (Sambrook, et al. *supra*). In a preferred embodiment the probes

and primers are synthesized by chemical synthesis methods (ed: Gait, M. J. 1984 *Oligonucleotide Synthesis*, IRL Press, Oxford, England).

5 One embodiment of the present invention provides nucleic acid primers that are complementary to *ceg* sequences, which allow the specific amplification of nucleic acid molecules of the invention or of any specific parts thereof. Another embodiment provides nucleic acid probes that are complementary for selectively or specifically hybridizing to the *ceg* sequences or to any part thereof.

10 **e) Derivative Nucleic Acid Molecules**

The nucleic acid molecules of the invention include peptide nucleic acids (PNAs), or derivative molecules such as phosphorothioate, phosphotriester, phosphoramidate, and methylphosphonate, that specifically bind to single-stranded DNA or RNA in a base pair-  
15 dependent manner (Zamecnik, P. C., et al., 1978 *Proc. Natl. Acad. Sci.* 75:280284; Goodchild, P. C., et al., 1986 *Proc. Natl. Acad. Sci.* 83:4143-4146).

PNA molecules comprise a nucleic acid oligomer to which an amino acid residue, such as lysine, and an amino group have been added. These small molecules, also designated  
20 anti-gene agents, stop transcript elongation by binding to their complementary (template) strand of nucleic acid (Nielsen, P. E., et al., 1993 *Anticancer Drug Des* 8:53-63). For example, reviews of methods for synthesis of DNA, RNA, and their analogues can be found in: *Oligonucleotides and Analogues*, eds. F. Eckstein, 1991, IRL Press, New York; *Oligonucleotide Synthesis*, ed. M. J. Gait, 1984, IRL Press, Oxford, England.  
25 Additionally, methods for antisense RNA technology are described in U. S. patents 5,194,428 and 5,110,802. A skilled artisan can readily obtain these classes of nucleic acid molecules using the herein described *ceg* polynucleotide sequences, see for example *Innovative and Perspectives in Solid Phase Synthesis* (1992) Egholm, et al. pp 325-328 or U. S. Patent No. 5,539,082.

30

### f) RNA Molecules

5 The present invention provides RNA molecules that encode the predicted *ceg* gene products. In particular, the RNA molecules of the invention may be isolated full-length or partial mRNA molecules or RNA oligomers that encode CEG gene products. The RNA molecules of the invention include the nucleotide sequences encoding all or portions of CEGs.

10 The RNA molecules of the invention also include antisense RNA molecules, peptide nucleic acids (PNAs), or non-nucleic acid molecules such as phosphorothioate derivatives, that specifically bind to the sense strand of DNA or RNA in a base pair-dependent manner. A skilled artisan can readily obtain these classes of nucleic acid molecules using the herein described *ceg* sequences.

15

### g) Labeled Nucleic Acid Molecules

The nucleic acid molecules having *ceg* sequences can be labeled with a detectable marker. Examples of a detectable marker include, but are not limited to, a radioisotope, a  
20 fluorescent compound, a bioluminescent compound, a chemiluminescent compound, a metal chelator or an enzyme. Technologies for generating labeled DNA and RNA probes are well known in the art (See e.g. Sambrook et al., *supra*).

## 2.) RECOMBINANT NUCLEIC ACID MOLECULES

25

Also provided are recombinant nucleic acid molecules, such as recombinant DNA molecules (rDNAs) that comprise *ceg* sequences or fragments thereof. As used herein, a recombinant DNA molecule is a DNA molecule that has been subjected to molecular manipulation *in vitro*. Methods for generating rDNA molecules are well known in the art, for example, see Sambrook  
30 et al., *Molecular Cloning* (1989), *supra*.

## a) Vectors

The nucleic acid molecules of the invention may be recombinant molecules each comprising the sequence, or portions thereof, of a *ceg* sequence linked to a non-*ceg* sequence. For example, the *ceg* sequence may be fused operatively to a vector to generate a recombinant molecule. The term vector includes, but is not limited to, plasmids, cosmids, and phagemids. A preferred vector includes an autonomously replicating vector comprising a replicon that directs the replication of the rDNA within the appropriate host cell. The preferred vectors can also include an expression control element, such as a promoter sequence, which enables transcription of the inserted *ceg* sequences and can be used for regulating the expression (e.g., transcription and/or translation) of an operably linked *ceg* sequence in an appropriate host cell such as *Escherichia coli*. Expression control elements are known in the art and include, but are not limited to, inducible promoters, constitutive promoters, secretion signals, enhancers, transcription terminators, and other transcriptional regulatory elements. Other expression control elements that are involved in translation are known in the art, and include the Shine-Dalgarno sequence, and initiation and termination codons. The preferred vector also includes at least one selectable marker gene that encodes a gene product that confers drug resistance such as resistance to ampicillin or tetracycline. The vector also comprises multiple endonuclease restriction sites that enable convenient insertion of exogenous DNA sequences.

The preferred vectors for generating *ceg* transcripts and/or the encoded CEG polypeptides are expression vectors which are compatible with prokaryotic host cells. Prokaryotic cell expression vectors are well known in the art and are available from several commercial sources. For example, a pET vectors (e.g., pET-21, Novagen Corp.) may be used to express CEG polypeptides in bacterial host cells.

### b) Recombinant Vectors for Integration

5 The present invention provides recombinant vectors that may be used to integrate exogenously provided sequences into the genome of a host cell. The recombinant integration vectors of the present invention include a gene that encodes a selectable marker and *ceg* sequences; or fragments thereof. The integration vectors are used to integrate the *ceg* sequence into a target gene sequence that resides within the bacterial host genome (e.g., endogenous sequence), thereby disrupting the function of the target gene sequence within the bacterial cells. These integration vectors may be used in a gene disruption assay to screen candidate *ceg* nucleotide sequences, in order to identify the candidate sequences that encode a gene product that is required for bacterial cell viability.

15 Accordingly, these recombinant integration vectors include candidate *ceg* sequences that will be screened to determine if the candidate *ceg* sequences encode a gene product that is required for cell viability. The candidate *ceg* sequence that is included as part of the recombinant integration vector is the "exogenous" *ceg* sequence that is employed as the "disrupting" sequence in a gene disruption assay. The *ceg* sequence that resides within the host genome is the "endogenous" or "target" *ceg* sequence.

20 The integration event rarely occurs, for example, by non-homologous recombination in which a recombinant vector, that includes the exogenous *ceg* sequence, inserts the exogenous *ceg* sequence into a random location within the host genome. In a more preferred embodiment, the integration event inserts the exogenous *ceg* sequence into a specific target site within the host genome. The targeted integration event can involve homologous recombination in which the integration vector, that includes the exogenous *ceg* sequence, inserts the exogenous *ceg* sequence into its homologous target *ceg* sequence that resides within the host's genome (e.g., the endogenous *ceg* sequence) (Figure 1). Further, the exogenous *ceg* sequence can be used as a disrupting sequence whereby the homologous recombination event integrates the exogenous *ceg* sequence into the endogenous target *ceg* sequence resulting in disruption of the function of the

endogenous *ceg* sequence. For example, disrupting the function of the endogenous *ceg* sequence may result in the loss of bacterial cell viability.

5 An example of a recombinant vector that can be used as an integration vector in *S. pneumoniae* is the pEVP-3 vector (Jean-Pierre Claverys, et al. 1995 *Gene* 164: 123-128). The pEVP-3 vector integrates an exogenous sequence by homologous recombination involving a Campbell-type event (S. Adhya and A. Campbell 1970 *J. Mol. Biol.* 50:481-490). The pEVP-3 vector includes a replicon that functions only in gram-negative bacteria, such as *E. coli*. Therefore, the pEVP-3 vector cannot replicate in *S.*  
10 *pneumoniae*. This vector also contains multiple cloning sites, and confers resistance to chloramphenicol in both a gram-negative and gram-positive bacteria, such as *S. pneumoniae*.

#### c) Fusion Gene Sequences

15

A fusion *ceg* gene is another example of a recombinant molecule of the invention. A fusion gene includes a *ceg* sequence operatively fused (e.g., linked) to a non-*ceg* sequence such as, for example, a tag sequence to facilitate isolation and/or purification of the expressed CEG gene product (Kroll, D.J., et al., 1993 *DNA Cell Biol* 12:441-53).

20

Alternatively, a recombinant fusion molecule has a *ceg* sequence of the invention fused to a *ceg* sequence isolated from a different microbial source. For example, the disclosed *ceg* sequences isolated from *S. pneumoniae* can be fused to a *ceg* sequence isolated from a different bacterial species.

25

### 3.) CEG PROTEINS AND POLYPEPTIDE MOLECULES

The invention additionally provides CEG proteins and peptide fragments thereof that are isolated or substantially purified. Embodiments of particular CEG amino acid sequences  
30 are disclosed in Tables I and II (SEQ ID NOS:114-226 and SEQ ID NOS:332-436, respectively).

The present invention also includes polypeptides having sequence variations from the predicted CEG polypeptide sequences disclosed herein, including mutant variants, conservative substitution variants, and similar CEG polypeptides from other prokaryotic organisms. For convenience, such proteins are referred to herein as "CEG proteins",  
5 "CEG polypeptides", or "proteins of the invention".

As used herein, CEG protein refers to a polypeptide having amino acid sequence identity or similarity to any one of the predicted amino acid sequences, as provided in SEQ ID NO.:  
10 114-226 or 332-436. The variant CEG polypeptides can be allelic forms of CEG, such as mutant forms of CEG polypeptides. The present invention also provides conservative substitution-mutants of the CEG proteins that maintain functional activity of wild-type CEG (e.g., the CEG polypeptide is required for bacterial cell viability).

15 The CEG protein may be isolated from any source whether natural, synthetic, semi-synthetic, or recombinant. As used herein, "natural" refers to a polypeptide which is found in nature. Accordingly, the CEG proteins may be isolated from a prokaryotic organism, such as a bacterial strain including, but not limited to, *Streptococcus*, *Escherichia*, *Bacillus*, *Pseudomonas*, *Yersinia*, *Salmonella*, and *Streptomyces*. The CEG  
20 proteins of the invention, and fragments thereof, can also be generated by recombinant methods or chemical synthesis methods.

The CEG polypeptides of the invention are essential for the viability of a bacterial cell. Further, the CEG polypeptides can exhibit at least any one of the following functions: a  
25 pantothenate kinase, a Holliday Junction branch migration protein, a single stranded DNA binding protein, a phosphoglucosamine mutase, an acetyltransferase, an uridylyltransferase, a malonyl CoenzymeA:ACP transacylase, a 3-oxoacyl-ACP synthase II, a 3-oxoacyl-ACP reductase, a phosphomethylpyrimidine (HMP-P) kinase, a GTP binding protein, a ATP binding protein, or a 4-aminoimidazole carboxylase. Putative  
30 functions can include, but are not limited to, sugar transferase, teichoic acid biosynthesis, ribosome recycling factor, response regulator, nicotinate phosphoribosyltransferase,



nitropropane dioxygenase, (3R)-hydroxymyristol acyl carrier protein dehydrase, sugar dehydrogenase, murein biosynthesis, cobalamin biosynthesis, ABC transporter, tRNA modification enzyme, arylsulfatase, 16S processing enzyme, tRNA methyl transferase, elongation factor P, signal recognition particle, protein export, undecaprenol kinase, SRP docking domain, diacyl glycerol kinase, dihydopicillinate reductase, HU-DNA binding protein, thiamine biosynthase, GreA transcription elongation factor, dTDP-L-rhamnose synthase, ATP-binding motif, ribose-5-p-3-epimerase-like activity, GTP pyrophosphokinase, acetyl-CoA carboxylase, O-sialoglycoprotein endopeptidase, glucosamine-fructose-6-phosphate aminotransferase, Strpn adhesion-associated ABC-permease, GTP pyrophosphokinase RelA, IMP dehydrogenase, DNA gyrase subunit B, acetyl-CoA carboxylase subunit AccD, phosphoglycerol kinase, acetyl-CoA carboxylase carbonyl transferase, phosphopanthetheine adenylyltransferase, oligopeptide transport permease subunit, translocation protein, perM permease, DNA pol III gamma and tau subunits, DNA pol III delta subunit, signal peptidase I, acetyl-coA carboxylase biotin carboxyl carrier protein, protein chain release factor-1, replicative DNA helicase, topoisomerase, pentapeptide-transferase, elongation factor G, spore coat polysaccharide biosynthesis protein C, protein release factor B, DNA polymerase III alpha subunit, phosphoprotein phosphatase, chaparonin, UDP-N-acetylmuramoylalanyl-D-glutamate-2, 6-diaminopimelate ligase, techuronic acid biosynthesis, UDP-glucose lipid carrier transferase, transcription termination factor, chromosome segregation factor, amino acid biosynthesis, HMG-CoA reductase, hypoxanthine-guanine phosphoribosyltransferase.

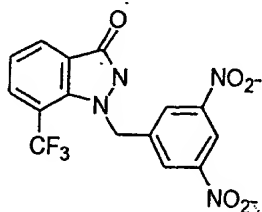
a) MODULATORS OF CEG POLYPEPTIDES

The invention provides compounds that modulate (e.g., activate or inhibit) the function of a CEG polypeptide. Such compounds can provide lead-compounds for developing drugs for diagnosing and/or treating conditions associated with bacterial infections. The modulator is a compound that may alter the function of the CEG polypeptide, such as activating or inhibiting the function of a CEG polypeptide. For example, the compound can act as agonist, antagonist, partial agonist, partial antagonist, cytotoxic agents,

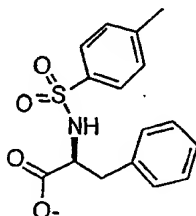
inhibitors of cell proliferation, and cell proliferation-promoting agents. The activity of the compound may be known, unknown or partially known.

5 Suitable ligands include, but are not limited to, diazalactones, *N*-protected amino acid, azabicyclodiene, and alkaloids.

An example of a diazalactone is:

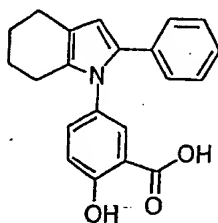


An example of a *N*-protected amino acid is:

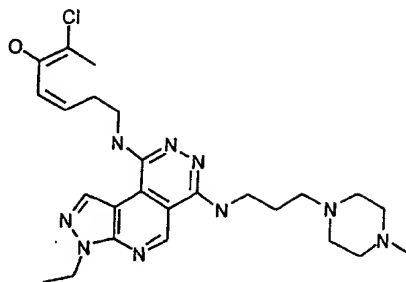
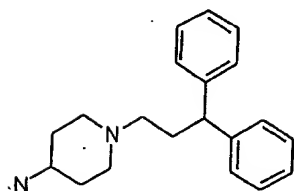
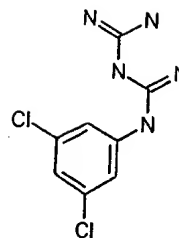
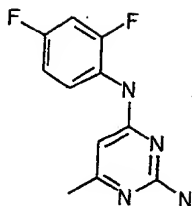
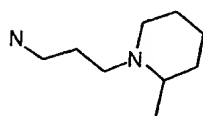


10

An example of an azabicyclodiene is:



Examples of alkaloids are:



## 5 B) METHODS FOR MAKING THE CEG PROTEINS AND POLYPEPTIDES

Recombinant methods are preferred if a high yield is desired. Recombinant methods involve expressing the cloned gene in a suitable host cell. For example, a host cell is introduced with an expression vector having the CEG sequence, then the host cell is cultured under conditions that permit *in vivo* production of the CEG protein. The recombinant vector can integrate the CEG sequence into the host genome. Alternatively, the CEG sequence can be maintained extra-chromosomally, as part of an autonomously replicating vector.

### 15 1. HOST-VECTOR SYSTEMS

The invention further provides a host-vector system comprising the vector, plasmid, phagemid, or cosmid comprising a *ceg* nucleotide sequence, or a fragment thereof, introduced into a suitable host cell. The host-vector system can be used to produce the

- CEG polypeptides encoded by the *ceg* nucleotide sequences. The host cell can be prokaryotic or eukaryotic. Examples of suitable prokaryotic host cells include bacteria strains from genera such as *Escherichia*, *Bacillus*, *Pseudomonas*, *Streptococcus*, and *Streptomyces*. Examples of suitable eukaryotic host cells include a yeast cell, a plant cell, or an animal cell, such as a mammalian cell. A preferred embodiment provides a host-vector system comprising the pET21 vector having a *ceg* sequence introduced into an *E. coli*  $\lambda$ DE3 lysogen which is useful, for example for the production of the CEG protein, herein designated CFE polypeptides and CFE proteins.
- 10 Introduction of the rDNA molecules of the present invention into an appropriate cell host is accomplished by well known methods that typically depend on the type of vector used and host system employed. For example, transformation of prokaryotic host cells by electroporation and salt treatment methods are typically employed, see for example, Cohen et al., 1972 *Proc Acad Sci USA* 69:2110; Maniatis, T., et al., 1989 *Molecular Cloning, A Laboratory Manual*, Cold Spring Harbor Laboratory, Cold Spring Harbor, NY.
- 15 Transformation of vertebrate cells with vectors containing rDNAs, electroporation, cationic lipid or salt treatment methods are typically employed, see, for example, Graham et al., 1973 *Virology* 52:456; Wigler et al., 1979 *Proc Natl Acad Sci USA* 76:1373-76.
- 20 Successfully transformed cells, i.e., cells that contain a rDNA molecule of the present invention, can be identified by well known techniques. For example, cells resulting from the introduction of a rDNA of the present invention can be selected and cloned to produce single colonies. Cells from those colonies can be harvested, lysed and their DNA content examined for the presence of the rDNA using a method such as that described by Southern, 25 *J Mol Biol* (1975) 98:503, or Berent et al., *Biotech* (1985) 3:208, or the proteins produced from the cell assayed via a biochemical assay or immunological method.
- Procaryotes are generally used as host cells for cloning and producing the products of exogenous DNA sequences. For example, the *Escherichia coli* K12 BL21 ( $\lambda$ DE3) (Novagen) is particularly useful for expression of foreign proteins. Other strains of *E. coli*, and bacilli such as *Bacillus subtilis*, Enterobacteriaceae such as *Salmonella*
- 30

*typhimurium* or *Serratia marcescans*, various *Pseudomonas*, *Streptococcus*, and *Streptomyces* species may also be employed as host cells in cloning and expressing the recombinant proteins of this invention.

- 5 In general terms, the production of recombinant CEG proteins may involve using a host/vector system, or other methods may be used. The host/vector system may employ the following steps.

10 A nucleic acid molecule is obtained that encodes a CEG protein or a fragment thereof, such as any one of the polynucleotides disclosed in SEQ ID NOs.: 1-113 or 227-331. The CEG-encoding nucleic acid molecule is preferably inserted into an expression vector in operable linkage with suitable expression control sequences, to generate an expression vector including the CEG-encoding sequence. The expression vector is introduced into a suitable host, by standard transformation methods, and the resulting transformed host is cultured  
15 under conditions that allow the production of the CEG protein. For example, if expression of the CEG gene is under the control of an inducible promoter, then suitable growth conditions would include the appropriate inducer. The CEG protein (e.g., designated a CFE polypeptide or protein), so produced, is isolated from the growth medium or directly from the cells; recovery and purification of the protein may not be necessary in some  
20 instances where some impurities may be tolerated. A skilled artisan can readily adapt an appropriate host/expression system known in the art for use with CEG-encoding sequences to produce a CEG protein (Cohen, et al., *supra*; Maniatis et al., *supra*).

25 Host cells harboring the nucleic acids disclosed herein are also provided by the present invention. A preferred host is *E. coli* strain BL21( $\lambda$ DE3) transfected or transformed with a vector comprising a nucleic acid of the present invention. The invention also provides a host cell capable of expressing the *ceg* sequences described herein. The preferred host cell is any strain of *E. coli* that can accommodate high level expression of an exogenously introduced gene.

30

The proteins of the present invention can also be made by chemical synthesis. The principles of solid phase chemical synthesis of polypeptides are well known in the art and may be found in general texts relating to this area (Dugas, H. and Penney, C. 1981 *Bioorganic Chemistry*, pp 54-92, Springer-Verlag, New York). CEG polypeptides may  
5 be synthesized by solid-phase methodology utilizing an Applied Biosystems 430A peptide synthesizer (Applied Biosystems, Foster City, Calif.) and synthesis cycles supplied by Applied Biosystems. Protected amino acids, such as t-butoxycarbonyl-protected amino acids, and other reagents are commercially available from many chemical supply houses.

10 The polypeptides of the invention exhibit properties of a CEG protein, such as, for example, the ability to elicit the generation of antibodies that specifically bind an epitope associated with CEG polypeptides. Accordingly, the CEG polypeptide, or any oligopeptide thereof, is capable of inducing a specific immune response in appropriate  
15 animals or cells and binding with specific antibodies.

**C) ANTIBODIES THAT RECOGNIZE AND BIND THE PROTEINS AND POLYPEPTIDES OF THE INVENTION**

20 The invention further provides antibodies (e.g., polyclonal, monoclonal, chimeric, humanized, and human antibodies) that bind a CEG polypeptide. The most preferred antibodies will selectively bind a CEG polypeptide and will not bind (or will bind weakly) a non-CEG polypeptide. Antibodies that are particularly contemplated include monoclonal and polyclonal antibodies, as well as fragments thereof (e.g., recombinant proteins) which  
25 include the antigen binding domain and/or one or more complement determining regions of these antibodies. These antibodies can be from any source, for example, rabbit, sheep, rat, dog, cat, pig, horse, mouse, and human.

The invention encompasses antibody fragments that specifically recognize a CEG  
30 polypeptide. As used herein, an antibody fragment is defined as at least a portion of the variable region of the immunoglobulin molecule that binds to its target, i.e., the antigen binding region. Some of the constant region of the immunoglobulin may be included.

As will be understood by those skilled in the art, the regions or epitopes of a CEG polypeptide to which an antibody is directed may vary with the intended application. For example, antibodies intended for use in an immunoassay for the detection of membrane-bound CEG proteins on viable bacterial cells should be directed to an accessible epitope on membrane-bound CEG proteins. Antibodies that recognize other epitopes may be useful for the identification of CEG protein within damaged or dying cells, for the detection of secreted CEG protein or fragments thereof.

Various methods for the preparation of antibodies are well known in the art. For example, antibodies may be prepared by immunizing a suitable mammalian host using a CEG protein, peptide, or fragment, in isolated or immunoconjugated form (Harlow, 1989 *Antibodies*, Cold Spring Harbor Press, NY). In addition, fusion proteins comprising CEG polypeptides may also be used, such as a CEG protein/GST-fusion protein. Cells expressing or overexpressing a CEG polypeptide may also be used for immunizations. Similarly, any cell engineered to express CEG protein may be used. This strategy may result in the production of monoclonal antibodies with enhanced capacities for recognizing endogenous CEG protein.

The present invention contemplates chimeric antibodies that comprise a human and non-human immunoglobulin portion. The antigen combining region (variable region) of a chimeric antibody can be derived from a prokaryotic source (e.g., bacteria) and the constant region of the chimeric antibody which confers biological effector function to the immunoglobulin can be derived from a eukaryotic source (e.g., human). The chimeric antibody should have the antigen binding specificity of the prokaryotic antibody molecule and the effector function conferred by the eukaryotic antibody molecule.

In one example, the procedure used to produce chimeric antibodies can involve the following steps:

- a) Identifying and cloning the correct immunoglobulin gene segment encoding the antigen binding portion of the antibody molecule. This gene segment is known as the VDJ, variable, diversity and joining regions for heavy chains or VJ, variable,

- joining regions for light chains or simply as the V or variable region. This gene regions may be in either the cDNA or genomic form;
- b) Cloning the gene segments encoding the constant region or desired part thereof;
  - c) Ligating the variable region with the constant region so that the complete chimeric antibody is encoded in a form that can be transcribed and translated;
  - d) Ligating this construct into a vector containing a selectable marker and gene control regions such as promoters, enhancers and poly(A) addition signals;
  - e) Amplifying this construct in bacteria;
  - f) Introducing this DNA into eukaryotic cells (transfection) most often mammalian lymphocytes;
  - g) Selecting for cells expressing the selectable marker;
  - h) Screening for cells expressing the desired chimeric antibody; and
  - k) Testing the antibody for appropriate binding specificity and effector functions.
- Chimeric antibodies of several distinct antigen binding specificities have been produced by protocols well known in the art, including anti-TNP antibodies (Boulianne et al., 1984 *Nature* 312:643); and anti-tumor antigen antibodies (Sahagan et al., 1986 *J. Immunol.* 137:1066). Likewise, several different effector functions have been achieved by linking new sequences to those encoding the antigen binding region. Examples of these include enzymes (Neuberger et al., 1984 *Nature* 312:604); immunoglobulin constant regions from another species and constant regions of another immunoglobulin chain (Sharon et al., 1984 *Nature* 309:364; Tan et al., 1985 *J. Immunol.* 135:3565-3567). Additionally, procedures for modifying antibody molecules and for producing chimeric antibody molecules using homologous recombination to target gene modification have been described (Fell et al., 1989 *Proc. Natl. Acad. Sci. USA* 86:8507-8511).

The predicted amino acid sequence of a CEG protein may be used to select specific regions of the CEG protein for generating antibodies. For example, hydrophobicity and hydrophilicity analyses of a CEG polypeptide may be used to identify hydrophobic and hydrophilic regions in the CEG protein. Regions of the CEG protein that show immunogenic structure, as well as other regions and domains, can readily be identified using



various other methods known in the art, such as Chou-Fasman, Garnier-Robson, Kyte-Doolittle, Eisenberg, Karplus-Schult or Jameson-Wolf analysis. Fragments that include the immunogenic regions are particularly suited for generating specific classes of antibodies.

- 5 Methods for preparing a protein for use as an immunogen and for preparing immunogenic conjugates of a protein with a carrier such as BSA, KLH, or other carrier proteins are well known in the art. In some circumstances, direct conjugation using, for example, carbodiimide reagents may be used; in other instances linking reagents such as those supplied by Pierce Chemical Co., Rockford, IL, may be effective. Administration of a CEG  
10 immunogen is conducted generally by injection over a suitable time period and with use of a suitable adjuvant, as is generally understood in the art. During the immunization schedule, titers of antibodies can be taken to determine adequacy of polyclonal antibody formation.

- While the polyclonal antisera produced in this way may be satisfactory for some  
15 applications, for pharmaceutical compositions, monoclonal antibody preparations are preferred. Immortalized cell lines which secrete a desired monoclonal antibody may be prepared using the standard method of Kohler and Milstein (*Nature* 256: 495-497) or other techniques as described in *Monoclonal Antibodies; A Manual of Techniques*, CRC press, Inc., Boca Raton, Fla. (1987) ed. Zola. The immortalized cell lines secreting the desired  
20 antibodies are screened by immunoassay in which the antigen is the CEG polypeptide having binding activity, or a fragment thereof. When the appropriate immortalized cell culture secreting the desired antibody is identified, the cells can be cultured either *in vitro* or by production in ascites fluid.

- 25 The desired monoclonal antibodies are then recovered from the culture supernatant or from the ascites supernatant. Fragments of the monoclonal antibodies of the invention or the polyclonal antisera (e.g., Fab, F(ab')<sub>2</sub>, Fv fragments, fusion proteins) which contain the immunologically significant portion (i.e., a portion that recognizes and binds a CEG protein) can be used as antagonists, as well as the intact antibodies. Humanized antibodies directed  
30 against a CEG polypeptide are also useful. The advantage of using humanized antibodies is that they are less immunogenic in humans. As used herein, a humanized antibody is an

- immunoglobulin molecule which is capable of binding to a CEG polypeptide and which comprises a FR region having substantially the amino acid sequence of a human immunoglobulin and a CDR having substantially the amino acid sequence of non-human immunoglobulin or a sequence engineered to bind a CEG protein. Methods for humanizing
- 5 murine and other non-human antibodies by substituting one or more of the non-human antibody CDRs for corresponding human antibody sequences are well known (Jones et al., 1986 *Nature* 321: 522-525; Riechman et al., 1988 *Nature* 332: 323-327; Verhoeyen et al., 1988 *Science* 239: 1534-1536; Carter et al., 1993 *Proc. Natl. Acad. Sci. USA* 89: 4285; and Sims et al., 1993 *J. Immunol.* 151: 2296).
- 10 Use of immunologically reactive fragments, such as the Fab, Fab', or F(ab')<sub>2</sub> fragments is often preferable, especially in a therapeutic context, as these fragments are generally less immunogenic than the whole immunoglobulin. Further, bi-specific antibodies specific for two or more epitopes may be generated using methods generally known in the art. Further,
- 15 antibody effector functions may be modified so as to enhance the therapeutic effect of the antibodies of the invention. For example, cysteine residues may be engineered into the Fc region, permitting the formation of interchain disulfide bonds and the generation of homodimers which may have enhanced capacities for internalization, ADCC and/or complement-mediated cell killing (Caron et al., 1992 *J. Exp. Med.* 176: 1191-1195; Shopes, 1992 *J. Immunol.* 148: 2918-2922). Homodimeric antibodies may also be
- 20 generated by cross-linking techniques known in the art (Wolff et al., *Cancer Res.* 53: 2560-2565). The invention also provides pharmaceutical compositions having the monoclonal antibodies or anti-idiotypic monoclonal antibodies of the invention.
- 25 The antibodies or fragments may also be produced, using current technology, by recombinant means. Regions that bind specifically to the desired regions of the CEG protein can also be produced in the context of chimeric or CDR grafted antibodies of multiple species origin. The invention includes an antibody, e.g., a monoclonal antibody which competitively inhibits the immunospecific binding of any of the monoclonal
- 30 antibodies of the invention to a CEG protein.

Alternatively, methods for producing fully human monoclonal antibodies, include phage display and transgenic methods, are known and may be used for the generation of human monoclonal antibodies (reviewed in: Vaughan et al., 1998 *Nature Biotechnology* 16: 535-539). For example, fully human monoclonal antibodies may be generated using cloning technologies employing large human Ig gene combinatorial libraries (i.e., phage display) (Griffiths and Hoogenboom, "Building an *in vitro* immune system: human antibodies from phage display libraries", in: *Protein Engineering of Antibody Molecules for Prophylactic and Therapeutic Applications in Man*, Clark, M. (Ed.), Nottingham Academic, pp 45-64 (1993); Burton and Barbas, "Human Antibodies from combinatorial libraries" *Id.*, pp 65-82). Fully human monoclonal antibodies may also be produced using transgenic mice engineered to contain human immunoglobulin gene loci as described in PCT Patent Application WO98/24893, Jakobovits et al., published December 3, 1997 (see also, Jakobovits, 1998 *Exp. Opin. Invest. Drugs* 7: 607-614). This method avoids the *in vitro* manipulation required with phage display technology and efficiently produces high affinity, authentic human antibodies.

The antibody or fragment thereof of the invention may be labeled with a detectable marker or conjugated to a second molecule, such as a therapeutic agent (e.g., a cytotoxic agent) thereby resulting in an immunoconjugate. For example, the therapeutic agent includes, but is not limited to, an anti-tumor drug, a toxin, a radioactive agent, a cytokine, a second antibody or an enzyme. Further, the invention provides an embodiment wherein the antibody of the invention is linked to an enzyme that converts a prodrug into a cytotoxic drug.

Examples of cytotoxic agents include, but are not limited to ricin, ricin A-chain, doxorubicin, daunorubicin, taxol, ethiduum bromide, mitomycin, etoposide, tenoposide, vincristine, vinblastine, colchicine, dihydroxy anthracin dione, actinomycin D, diphtheria toxin, *Pseudomonas* exotoxin (PE) A, PE40, abrin, arbrin A chain, modeccin A chain, alpha-sarcin, gelonin, mitogellin, retstrictocin, phenomycin, enomycin, curicin, crotin, calicheamicin, sapaonaria officinalis inhibitor, and glucocorticoid and other chemotherapeutic agents, as well as radioisotopes such as  $^{212}\text{Bi}$ ,  $^{131}\text{I}$ ,  $^{131}\text{In}$ ,  $^{90}\text{Y}$ , and  $^{186}\text{Re}$ .

Suitable detectable markers for diagnostic used include, but are not limited to, a radioisotope, a fluorescent compound, a bioluminescent compound, chemiluminescent compound, a metal chelator or an enzyme. Antibodies may also be conjugated to an anti-  
5 cancer pro-drug activating enzyme capable of converting the pro-drug to its active form. See, for example, U.S. Patent Nos. 4,952,394 and 5,716,990.

Additionally, a recombinant protein of the invention comprising the antigen-binding region of any of the monoclonal antibodies of the invention can be made. In such a  
10 situation, the antigen-binding region of the recombinant protein is joined to at least a functionally active portion of a second protein having therapeutic activity. The second protein can include, but is not limited to, an enzyme, lymphokine, oncostatin or toxin. Suitable toxins include those described above.

15 Techniques for conjugating or joining therapeutic agents to antibodies are well known (Arnon et al., "Monoclonal Antibodies For Immunotargeting Of Drugs In Cancer Therapy", in: *Monoclonal Antibodies And Cancer Therapy*, Reisfeld et al. (eds.), pp. 243-56, Alan R. Liss, Inc. 1985; Hellstrom et al., "Antibodies For Drug Delivery", in: *Controlled Drug Delivery* (2nd Ed.), Robinson et al. (eds.), pp. 623-53, Marcel Dekker, Inc. 1987; Thorpe,  
20 "Antibody Carriers Of Cytotoxic Agents In Cancer Therapy: A Review", in: *Monoclonal Antibodies '84: Biological And Clinical Applications*, Pinchera et al. (eds.), pp. 475-506 (1985); and Thorpe et al., "The Preparation And Cytotoxic Properties Of Antibody-Toxin Conjugates", in: *Immunol. Rev.*, 62:119-58 (1982)). Techniques for joining detectable markers to antibodies are also known.

25

#### D) PHARMACEUTICAL COMPOSITIONS OF THE INVENTION

The invention includes pharmaceutical compositions for use in the treatment of microbial infections comprising a pharmaceutically effective amount of an anti-CEG antibody or a  
30 CEG polypeptide.

In one embodiment, the pharmaceutical compositions may comprise a CEG antibody, either unmodified, conjugated to a therapeutic agent (e.g., drug, toxin, enzyme or second antibody) or in a recombinant form (e.g., chimeric or bispecific). The compositions may additionally include other antibodies or conjugates (e.g., an antibody cocktail).

5

The pharmaceutical compositions also preferably include suitable carriers and adjuvants which include any material which when combined with the molecule of the invention (e.g., an anti-CEG antibody or a CEG protein) retains the molecule's activity and is non-reactive with the subject's immune systems. Examples of suitable carriers and adjuvants include, but are not limited to, human serum albumin, ion exchangers, alumina, lecithin, buffer substances such as phosphates, glycine, sorbic acid, potassium sorbate, and salts or electrolytes such as protamine sulfate. Other examples include any of the standard pharmaceutical carriers such as a phosphate buffered saline solution, water, emulsions such as oil/water emulsion, and various types of wetting agents. Other carriers may also include sterile solutions, tablets including coated tablets and capsules. Typically such carriers contain excipients such as starch, milk, sugar, certain types of clay, gelatin, stearic acid or salts thereof, magnesium or calcium stearate, talc, vegetable fats or oils, gums, glycols, or other known excipients. Such carriers may also include flavor and color additives or other ingredients. Compositions comprising such carriers are formulated by well known conventional methods. Such compositions may also be formulated within various lipid compositions, such as, for example, liposomes as well as in various polymeric compositions, such as polymer microspheres.

The pharmaceutical compositions of the invention can be administered using conventional modes of administration including, but not limited to, intravenous, intraperitoneal, oral, intralymphatic or administration directly into the tumor. Intravenous administration is preferred.

The pharmaceutical compositions of the invention may be in a variety of dosage forms which include, but are not limited to, liquid solutions or suspensions, tablets, pills, powders, suppositories, polymeric microcapsules or microvesicles, liposomes, and

injectable or infusible solutions. The preferred form depends upon the mode of administration and the therapeutic application.

5 The CEG polypeptides and proteins of this invention are found in common pathogenic bacterial species such as *Streptococcus pneumoniae*. This organism causes upper respiratory tract infections. Thus, the peptides and proteins of this invention can be used as immunogens in subunit vaccines for vaccination against a pathogenic bacteria such as *Streptococcus pneumoniae*. Additionally, the *ceg* sequences of the invention can be used as DNA vaccines (U.S. Patent No. 5,736,524 and U.S. Patent No. 5,989,553).

10

The polypeptides and proteins of this invention can be formulated as univalent and multivalent vaccines. The protein can be mixed, conjugated or fused with other antigens, including B or T cell epitopes of other antigens.

15 Further, when a haptenic peptide of the proteins of the invention is used, (i.e., a peptide which reacts with cognate antibodies, but cannot itself elicit an immune response), it can be conjugated to an immunogenic carrier molecule. Conjugation to an immunogenic carrier can render the oligopeptide immunogenic. Examples of carrier molecules are tetanus toxin or toxoid, diphtheria toxin or toxoid and any mutant forms of these proteins  
20 such as CRM.sub.197. Others include exotoxin A of *Pseudomonas*, the heat labile toxin of *E. coli* and rotaviral particles (including rotavirus and VP6 particles). Alternatively, a fragment or epitope of the carrier protein or other immunogenic protein can be used. For example, the hapten can be coupled to a T cell epitope of a bacterial toxin.

25 In formulating the vaccine compositions with the CEG polypeptides or proteins of the invention, alone or in the various combinations described, the immunogen is adjusted to an appropriate concentration and formulated with any suitable vaccine adjuvant. Suitable adjuvants include, but are not limited to: surface active substances, e.g., hexadecylamine, octadecylamine, octadecyl amino acid esters, lysolecithin, dimethyl-  
30 dioctadecylammonium bromide), methoxyhexadecylglycerol, and pluronic polyols; polyamines, e.g., pyran, dextran sulfate, poly. IC, carbopol; peptides, e.g., muramyl

dipeptide, dimethylglycine, tuftsin; oil emulsions; and mineral gels, e.g., aluminum hydroxide, aluminum phosphate, etc. and immune stimulating complexes. The immunogen may also be incorporated into liposomes, or conjugated to polysaccharides and/or other polymers.

5

The vaccines can be administered to a human or animal in a variety of ways. These include intradermal, intramuscular, intraperitoneal, intravenous, subcutaneous, oral and intranasal routes of administration. Further, the vaccines can be live or inactivated vaccines.

10

The most effective mode of administration and dosage regimen for the compositions of this invention depends upon the severity and course of the disease, the patient's health and response to treatment and the judgment of the treating physician. Accordingly, the dosages of the compositions should be titrated to the individual patient.

15

#### E) USES OF THE MOLECULES OF THE INVENTION

##### 1) MOLECULAR WEIGHT MARKERS

20 The nucleic acid molecules of the invention and their encoded proteins may be employed as molecular weight markers. For example, the molecular weight of each of the nucleic acid molecules having *ceg* sequences and their predicted polypeptides can be determined and can be used to compare against other gene sequences and proteins whose molecular weights are unknown.

25

##### 2) DIAGNOSTICS

The nucleic acid molecules of the invention may be employed in diagnostic embodiments. For example, the presence of nucleotide sequences which are identical or  
30 similar to the *ceg* sequences of the invention may be detected within a biological sample.

The biological sample may include blood, serum or a swab from nose, ear or throat, may be determined by means of a nucleic acid detection assay.

5 Nucleic acid probes or primers having sequences complementary to *ceg* sequences may be used in a hybridization assay to detect the presence of the sequences which are identical or similar to the *ceg* sequences of the invention in the biological samples. Typically, nucleic acids molecules obtained from a suitable biological sample are hybridized with labeled probes or primers. The resulting hybridized molecules are detected and resolved by methods well known in the art, such as Northern or Southern blotting, micro-array technology, or amplifying with PCR technology. Other hybridization techniques and systems are known that can be used in connection with the detection aspects of the invention, including diagnostic assays such as those described in Falkow et al., U.S. Pat. No. 4,358,535.

15 Examples of the PCR technology are disclosed in U.S. Patent Nos. 4,683,202 and 4,965,188 (incorporated herein by reference). Generally, nucleic acid molecules are obtained from a suitable biological source and contacted with two primers corresponding to the *ceg* sequences disclosed herein, under conditions which allow for hybridization and polymerization to occur. A pair of probes, one corresponding to the 5' flanking region and the other corresponding to the 3' flanking region, would be sufficient to detect the nucleic acid molecules of the invention in a biological sample and may be used to indicate the amount of bacteria present.

25 Alternative methods of detecting nucleic acid molecules include, for example, in situ hybridization techniques, where a *ceg* probe is used to detect homologous sequences within one or more cells, such as cells within a clinical sample or even cells grown in tissue culture. As is well known in the art, the cells are prepared for hybridization by fixation, e.g. chemical fixation, and placed in conditions that allow for the hybridization of a detectable probe with nucleic acids located within the fixed cell.

30



The amount of *ceg* sequences present in a biological sample can be quantified and compared to the levels in a normal or "healthy" sample. For example, *ceg* sequences present in either increased or decreased levels, compared to the levels found in the control sample may indicate the presence of bacteria. This information is useful for  
5 diagnosis of a bacterial infection that requires treatment with an antibacterial agent.

Alternatively, the amount of CEG polypeptides present in a biological sample may be determined by means of an immunoassay. For example, labeled antibodies reactive against CEG polypeptides may be used in an immuno-reactive assay to detect the  
10 presence of CEG polypeptides in the biological samples.

### 3) SCREENING CANDIDATE CEG SEQUENCES

#### a) Gene Disruption Assay

15 The *ceg* nucleotide sequences of the invention can be used to identify nucleotide sequences which are identical or similar to the *ceg* sequences that are required for bacterial cell viability. For example, the *ceg* sequences can be used in a bacterial gene disruption assay to screen candidate nucleotide sequences to identify sequences required  
20 for bacterial cell viability.

The disruption assay can involve: introducing into a host cell a recombinant vector that is capable of integration into the host genome, where the recombinant vector includes a candidate sequence that putatively encodes a cell-viability gene product (e.g., the  
25 exogenous *ceg* sequence); the vector integrates the candidate sequence into a target sequence within the host's genome (e.g., the endogenous *ceg* sequence); and the host cell, so introduced, is screened for viability. The recombinant vector preferably includes a selectable marker so that the introduced host cell can be screened for viability in the presence of a selectable agent.

30

For example, Figure 1 shows a schematic representation of a gene disruption assay, within a bacterial host cell. In Figure 1A, the recombinant vector, pEVP3, includes the CAT gene (e.g., the selectable marker chloramphenicol acetyl transferase) and an internal region of the *ceg* disrupting sequence; the internal region excludes the 5' and 3' ends of the *ceg* sequence. The "X" in Figure 1 indicates the recombinant pEVP3 vector undergoing homologous recombination with the target sequence (e.g., within the host genome). In Figure 1B, the resolved pEVP3 vector that is integrated into the host genome, is shown. Left to right are the following elements: the native promoter of the target gene; a 5' partial copy of the target gene; the body of the integrated pEVP3 vector including the disrupting gene and CAT; and, a 3' partial copy of the target gene. Thus, integration of the pEVP3 vector via homologous recombination results in two partial gene duplications flanking the integrated vector. If the target gene is not essential for survival, it is possible to recover chloramphenicol-resistant colonies of *S. pneumoniae*. Failure to recover chloramphenicol resistant colonies, in the presence of the proper controls as described below, indicates that the target gene may be essential for cell viability.

More particularly, the gene disruption assay for screening candidate *ceg* sequences can involve the following steps. The recombinant pEVP-3 vector encoding CAT resistance and having a fragment of a candidate *ceg* sequence, can be introduced into transformation-competent *S. pneumoniae* cells by methods that are well-known in the art (Lee, M.S., et al., 1998 *Appl. Environ. Microbiol.* 64:4796-4802). The preferred size of the *ceg* fragment can be between about 200 to about 500 bp in length. It is advantageous that the candidate *ceg* sequence does not include the 5' and 3' ends that encode the N- and C-terminal ends of the CEG polypeptide. This insures that the inserted *ceg* fragment and the disrupted endogenous *ceg* gene sequence are not capable of expression of a full-length, functional *ceg* gene product. The transformation-competent cells can be obtained by performing the transformation step in the presence of a heptadecapeptide that induces competence for transformation of *S. pneumoniae* (Havarstein, L. S., et al., 1995 *Proc. Nat'l. Acad. Sci.* 92:11140-11144), such as the CSP-1 peptide. The CSP-1 can be naturally-derived or synthetic. Additionally, the transformation step can be optimized by performing the transformation when the cells have reached a density which is optimal for

transformation (e.g.,  $3 \times 10^7$  cells per ml.) (Havarstein, L. S. et al. *supra*). The recombinant vector can be introduced into the competent pneumococci and may undergo homologous recombination, whereby the candidate *ceg* fragment recombines with the corresponding endogenous *ceg* sequence, resulting in targeted integration of the vector into the pneumococcal genome and disruption of the endogenous *ceg*.

The transformed cells can be plated on or cultured in chloramphenicol-containing growth medium. The cells can be cultured under standard conditions, such as 37° C in 5% CO<sub>2</sub> for approximately 40 to 48 hours, for the purpose of selecting cells that carry the integrated vector.

Additionally, control samples can be run in parallel with the gene disruption assay, in order to determine whether the gene disruption procedure is working properly. For example, the control samples can be used to calibrate the gene disruption experiment so that disruption of a known non-essential bacterial gene results in an approximate number of colonies per plate. Similarly, the disruption of a known essential gene can be calibrated to yield only zero or one colony per plate. The appearance of one colony is due to the rare illegitimate recombination into a non-homologous sequence. In particular, a known non-essential gene such as the *lytA* gene (Tomasz, A., et al., 1988 *J. Bacteriol.* 170:5931-5934) can be used so that between about 70 to 100 chloramphenicol-resistant colonies will grow per plate. Similarly, the *ftsZ* gene (Lutkenhaus, J. F., et al., 1980 *J. Bacteriol.* 143:1281-1288), a known essential gene, can be used to yield zero or, rarely, one colony per plate. As is well known in the art, specific parameters that are involved in any given gene disruption assay can be adjusted to calibrate the desired number of plated cells in the control samples. Experimental parameters that can be adjusted include, but are not limited to, the *E. coli* strain used to propagate the vector/insert, the fragment length of the sequence to be integrated, the amount of recombinant integration vector used to transform the cells, use of transformation-competent cells, and plating density of the transformed cells.

30

The transformed cells carrying the recombinant integration vector that disrupts expression of an endogenous essential gene (e.g., the target *ceg* gene) can be identified, based on a selectable phenotype such as non-viability. For example, the cells that carry a disrupted non-essential gene will be viable and, due to the integration of pEVP3, will grow on chloramphenicol-containing medium. In contrast, cells that carry a disrupted essential gene will not grow (e.g., non-viable) on the chloramphenicol-containing medium. Thus, the transformed cells that do not grow under these selective conditions carry an endogenous gene sequence that is essential for cell viability which has been disrupted by an exogenous candidate fragment, thereby identifying a *ceg* sequence. Steps one through three may be repeated in order to confirm that the *ceg* sequences, so identified, are essential for cell viability.

#### b) Autolysin Assay

It is advantageous to perform additional steps to determine whether the homologous recombination events result in disruption of the intended target gene sequence. The *lytA* transformation control can be used to confirm that the transformation system is functioning properly. For example, a phenotypic test for autolysin activity (*lytA* gene product) can be performed to determine that the exogenous *lytA* fragment is correctly integrated into the *lytA* site within the host genome. This typically involves flooding the culture plates containing transformants carrying the integrated *lytA* control vector with a solution of detergent, such as 0.1% deoxycholate, which triggers cell lysis in *lytA*-intact cells (e.g., the cells that have not undergone homologous recombination). After about 5-10 minutes the colonies with intact *lytA* will appear ghost-like due to cell lysis, and the colonies with a disrupted *lytA* gene will appear intact.

#### c) Polarity Analysis

The *ceg* sequences that are confirmed to be essential for cell viability can be examined further by performing a polarity analysis to determine if the corresponding endogenous *ceg* sequence is organized in an operon. Polarity is an effect unique to prokaryotes and is

the result of the operon organization of bacterial genomes. Many bacterial genes are arranged in operons in which multiple genes are under the control of a single regulatory sequence (e.g., a promoter) and are transcribed into a single mRNA transcript. With respect to the orientation of multiple genes within an operon, the genes that are proximal to the regulatory sequence are said to be "upstream" genes and the genes that are distal are said to be "downstream" genes. For example, many operons contain genes encoding different proteins that catalyze discrete steps of a common biochemical pathway. Thus, any of the proteins that catalyze the steps of the pathway may be essential for cell viability.

5

The presence of operons in a bacterial host genome may influence the interpretations of the gene disruption results. For example, disruption of an upstream gene may be erroneously interpreted as affecting the expression of the disrupted gene but may, in fact, have expression effects on the intact downstream genes. Therefore, it is advantageous to perform a polarity analysis to determine if a *ceg* sequence is part of an operon.

10

A polarity analysis can involve performing an *in vivo* gene disruption procedure using, as the disrupting sequence, a *ceg* sequence that includes the entire *ceg* coding sequence region but lacking expression regulatory sequences. This differs from the gene disruption assay, which involves the central region of the *ceg* sequence. The polarity analysis involves gene duplication via homologous recombination. For example, the pEVP-3 vector having the entire coding region of a *ceg* sequence can be used for the polarity analysis (Figure 2 A). The polarity analysis will yield different results depending on the organization of the endogenous target sequence within the host genome.

15

20

For example, Figure 2 shows a schematic representation of the polarity test for operons, within a bacterial host cell. In Figure 2A, the recombinant vector, pEVP3, includes the CAT gene and the entire coding region of the *ceg* disrupting sequence. The "X" in Figure 2 indicates the recombinant pEVP3 vector undergoing homologous recombination with the target sequence. Two of the possible results of homologous recombination are shown in Figures 2 B and C.

25

30

In Figure 2 B, case 1, if the endogenous target sequence is not organized in an operon, the integration event may yield: a functional target sequence (e.g., it is capable of expression); a duplicate non-functional target sequence that lacks a promoter; and a functional downstream gene (e.g., Gene B) that is controlled by its own promoter. The cells carrying this type of integrated target sequence can be recovered as viable cells that grow in the presence of chloramphenicol; this condition is termed "polarity negative".

In Figure 2 C, case 2, if the target sequence is organized in an operon, then the integration event may yield an integration site that is similar to that described for case 1, including: a functional target sequence; and a duplicate non-functional target sequence which is not functional. However, this integration event may also yield a non-functional downstream gene (e.g., Gene B) because expression of this downstream gene is controlled by a promoter located upstream of the insertion site. The cells that carry this type of integrated target sequence will be non-viable; this condition is termed "polarity positive". Thus, the polarity analysis provides a method to determine whether integration of a recombinant vector into a target *ceg* sequence effects expression of downstream genes.

The *ceg* sequences disclosed herein (SEQ ID NOs.: 1-113, 227-331) encode gene products that are essential for viability in *S. pneumoniae*. Furthermore, many of these *ceg* sequences have been analyzed for the polarity effect and the results are presented in Table I. One subset of *ceg* sequences is classified as polarity negative (-), since the homologous recombination event did not effect the expression of downstream genes. Another subset of *ceg* sequences is classified as polarity positive (+), since the homologous recombination event did affect the expression of downstream genes. The *ceg* sequences that have not yet been classified as polarity positive or negative are indicated in Table I as a blank. For the *ceg* sequences that are classified as polarity positive, the genes downstream of the disrupted endogenous *ceg* sequences may or may not also be essential.

#### 4) ASSAYS FOR IDENTIFYING CEG LIGANDS AND OTHER BINDING AGENTS

- The present invention provides screening methods for identifying agents that interact and/or bind to the CEG proteins of the invention, such as a ligand. An agent can be, for example, a natural product, a derived or synthetic chemical molecule, a polypeptide, a nucleic acid molecule, or a metal. The agents that interact with CEG proteins may cause bacterial cell death by disrupting the functions of CEG proteins, including, but not limited to, nucleotide biosynthesis, DNA replication, RNA transcription, protein translation, and/or cell wall biosynthesis. Accordingly, the present invention provides screening methods for identifying agents having antibacterial activity, such as agents that cause bacterial cell death by interacting with the CEG proteins. These antibacterial agents are useful for treating diseases and afflictions associated with bacterial infections.
- Various methods can be used to discover agents having antibacterial activity, as determined by the ability of the binding agent to bind to a CEG protein and disrupt the function of the CEG protein. These screening methods include whole cell *in vivo* assays as well as *in vitro* assays with cellular components.
- An *in vivo* screening method for identifying ligands that bind CEG polypeptides can be performed in a whole cell assay. A typical method may be the use of whole bacterial cells to assess the antibacterial properties based on cell growth or viability. These methods can include methods for measuring cell growth and/or viability, for example, by optical density or zones of growth (Koch, A. L. et al., 1970 *Anal. Biochem.* 38:252-259; Biemer, J. J. et al., 1973 *Ann. Clin. Lab. Sci.* 2:135-140; *Manual of Clinical Microbiology*, 7<sup>th</sup> edition, Murray, P. R. (ed), ASM Press), by growth inhibition in an agar assay (Murray, P. R., *supra*), or other means of detecting cell metabolism (Mychajlonka, M. et al., 1980 *Antimicrob. Agents Chemother.* 17:572-582), and are well known to those skilled in the art. In addition, there are molecular biology-based detection methods for use with whole bacterial cells, such as gene reporter assays, to monitor the effect of the ligand on specific targets (Slauch, J. M., et al., 1991 *Methods Enzymol.* 204:213-248). Examples of the reporter genes include, but are not limited to, beta-

galactosidase, alkaline phosphatase, luciferase, and green fluorescent protein. For example, one embodiment provides a reporter system that monitors inhibition of DNA synthesis by fusing a reporter such as beta-galactosidase (*lacZ*) to genes known to be upregulated by the cessation of DNA synthesis as a result of the binding of ligands to the DNA synthetic apparatus. (Shurvinton, C. E., et al., 1982 *Mol. Gen. Genetics* 185:352-355; Rosato, A., et al., 1998 *Antimicrob. Agents Chemother.* 42:1392-1396).

Alternatively, the yeast two-hybrid system (Fields, S. and Song, O. 1989, *Nature* 340:245-246) may be adapted to screen for ligands that bind CEG polypeptides. Generally, the yeast two-hybrid system is performed in a yeast host cell carrying a reporter gene, and is based on the modular nature of the GAL transcription factor which has a DNA binding domain and a transcriptional activation domain. The yeast two-hybrid system relies on the physical interaction between a recombinant polypeptide that comprises the GAL DNA binding domain and another recombinant polypeptide that comprises the GAL transcriptional activation domain. The physical interaction between the two recombinant polypeptides reconstitutes the transcriptional activity of the transcription factor, thereby causing expression of the reporter gene. Either of the recombinant polypeptides used in the two-hybrid system can be generated to include a CEG polypeptide sequence to screen for binding partners of CEG.

Another method uses the bacterial CEG proteins as the basis for *in vitro* assay systems to detect binding agents. Typically, the *in vitro* screening method comprises: a) generating the CEG protein of the invention, or membranes enriched in the CEG protein; b) exposing the CEG protein or membranes to a candidate agent; and c) detecting the interaction of the CEG protein with the agent by any suitable means. Additionally, the screening methods may be adapted to automated high-throughput procedures, such as PANDEX.RTM Baxter-Dade Diagnostics, allowing for efficient high-volume screening of candidate agents.

An alternative method for screening potential ligands involves an *in vitro* binding procedure. Typically, the CEG proteins of the invention can be produced using



recombinant DNA technology and host-vector systems as described herein. A candidate agent is introduced into a reaction vessel containing the CEG protein, or fragment thereof; the candidate agents may be detectable by methods such as, but not limited to, radioisotope or chemical labeling. Binding of the CEG protein by a candidate agent can  
5 be determined by any suitable means, including, for example, quantifying bound label versus unbound label using any suitable method. Binding of a candidate agent may also be detected by methods similar to an alternative physical method disclosed in U.S. Patent No. 5,585,277. In this method, binding of a candidate agent to a protein is assessed by monitoring the ratio of folded protein to unfolded protein, for example by monitoring  
10 sensitivity of the protein to a protease, or amenability to binding of the protein by a specific antibody against the folded state of the protein, or binding to chaperone protein, or by binding to any suitable surface.

The invention provides methods of identifying compounds that modulate (e.g., activate or  
15 inhibit) the function of a CEG polypeptide. Essentially any compound can be used in the assays of the invention. The preferred compounds are those that are soluble in aqueous or organic solutions. It will be appreciated by those of skill in the art that there are many commercial suppliers of chemical compounds that can be used in the methods of the invention, including Sigma Chemical Co. (St. Louis, Mo.), Aldrich Chemical Co. (St.  
20 Louis, Mo.), Sigma-Aldrich (St. Louis, Mo.), Fluka Chemika-Biochemica Analytika (Buchs, Switzerland), and the like.

The present invention provides methods for detecting compounds which are identified as modulators of CEG function. The methods of the invention can be performed using  
25 isolated CEG polypeptides, or use whole cells expressing the CEG polypeptide. The steps of the method using isolated CEG polypeptides include: contacting the isolated CEG polypeptide with a candidate compound; and determining whether the function of the CEG polypeptide is altered. The steps of the method using whole cells include: contacting the whole cells with a candidate compound; and determining whether the cell  
30 dies, indicating the compound inhibited the function of a CEG polypeptide.

The preferred methods of the invention provide high-throughput screening assays for identifying compounds which modulate the function of a CEG polypeptide. The high throughput methods permit screening of large libraries of compounds. For example the high throughput methods can use automated assay steps. The assays can be performed  
5 in parallel on a solid support, as microtiter formats on microtiter plates in robotic assays are well known. A preferred embodiment of the methods includes adapting the methods to use microtiter plates or pico- nano- or micro-liter arrays. In high throughput assays it is desirable to run positive controls to ensure that the components of the assays are working properly.

10

The high throughput screening methods of the invention include providing a combinatorial library containing a large number of compounds (candidate modulator compounds) (Borman, S, C. & *E. News*, 1999, 70(10), 33-48). Such combinatorial chemical libraries can be screened in one or more assays to identify library members  
15 (particular chemical species or subclasses) that exhibit the ability to modulate the function of the CEG polypeptide (Borman, S., *supra*; Dagani, R. C. & *E. News*, 1999, 70(10), 51-60). The compounds, so identified, can serve as lead-compounds or can themselves be used as potential or actual therapeutics.

20 A combinatorial chemical library is a collection of diverse chemical compounds generated by using either chemical synthesis or biological synthesis, to combine a number of chemical building blocks, such as reagents. For example, a linear combinatorial chemical library, such as a polypeptide library, is formed by combining a set of chemical building blocks (amino acids) in every possible way for a given  
25 compound length (i.e., the number of amino acids in a polypeptide compound). Millions of chemical compounds can be synthesized through such combinatorial mixing of chemical building blocks.

Preparation and screening of combinatorial chemical libraries is well known to those of skill in  
30 the art. Such combinatorial chemical libraries include, but are not limited to, peptide libraries (see, e.g., U.S. Pat. No. 5,010,175, Furka, *Int. J. Pept. Prot. Res.*, 1991, 37:487-493 and

Houghton, et al., *Nature*, 1991, 354, 84-88). Other chemistries for generating chemical diversity libraries can also be used. Such chemistries include, but are not limited to, peptoids (PCT Publication No. WO 91/19735); encoded peptides (PCT Publication WO 93/20242); random bio-oligomers (PCT Publication No. WO 92/00091); benzodiazepines (U.S. Pat. No. 5,288,514); diversomers, such as hydantoins, benzodiazepines and dipeptides (Hobbs, et al., *Proc. Nat. Acad. Sci. USA*, 1993, 90, 6909-6913); vinylogous polypeptides (Hagihara, et al., *J. Amer. Chem. Soc.* 1992, 114, 6568); nonpeptidal peptidomimetics with *beta*-D-glucose scaffolding (Hirschmann, et al., *J. Amer. Chem. Soc.*, 1992, 114, 9217-9218); analogous organic syntheses of small compound libraries (Chen, et al., *J. Amer. Chem. Soc.*, 1994, 116, 2661; Armstrong, et al. *Acc. Chem. Res.*, 1996, 29, 123-131); or small organic molecule libraries (see, e.g., benzodiazepines, Baum *C&E News*, 1993, Jan. 18, page 33,); oligocarbamates (Cho, et al., *Science*, 1993, 261, 1303); and/or peptidyl phosphonates (Campbell, et al., *J. Org. Chem.* 1994, 59, 658); nucleic acid libraries (see, Seliger, H et al., *Nucleosides & Nucleotides*, 1997, 16, 703-710); peptide nucleic acid libraries (see, e.g., U.S. Pat. No. 5,539,083); antibody libraries (see, e.g., Vaughn, et al., *Nature Biotechnology*, 1996, 14(3), 309-314 and PCT/US96/10287); carbohydrate libraries (see, e.g., Liang, et al., *Science*, 1996, 274, 1520-1522 and U.S. Pat. No. 5,593,853, Nilsson, UJ, et al., *Combinatorial Chemistry & High Throughput Screening*, 1999 2, 335-352; Schweizer, F; Hindsgaul, O. *Current Opinion In Chemical Biology*, 1999 3, 291-298); isoprenoids (U.S. Pat. No. 5,569,588); thiazolidinones and metathiazanones (U.S. Pat. No. 5,549,974); pyrrolidines (U.S. Pat. Nos. 5,525,735 and 5,519,134); morpholino compounds (U.S. Pat. No. 5,506,337); benzodiazepines (U.S. Pat. No. 5,288,514); and other similar art.

Devices for the preparation of combinatorial libraries are commercially available (see, e.g., 357 MPS, 390 MPS, Advanced Chem. Tech, Louisville Ky., Symphony, Rainin, Woburn, Mass., 433A Applied Biosystems, Foster City, Calif., 9050 Plus, Millipore, Bedford, Mass.). In addition, numerous combinatorial libraries are themselves commercially available (see, e.g., ComGenex, Princeton, N.J., Asinex, Moscow, Ru, Tripos, Inc., St. Louis, Mo., ChemStar, Ltd., Moscow, RU, 3D Pharmaceuticals, Exton, Pa., Martek Bio sciences, Columbia, Md., etc.).

In the high throughput methods of the invention, several thousand different candidate compounds can be screened in a relatively short period of time. For example, each well of a microtiter plate can be used to run a separate assay against a selected potential modulator, or if concentration or incubation time effects are to be observed, every 5-10 wells can test a single modulator. Thus, a single standard microtiter plate can assay about 100 (96) modulators. If 1536 well plates are used, then a single plate can easily assay from about 100 to about 1500 different compounds. It is possible to assay many different plates per day; assay screens for up to about 6,000-20,000, and even up to about 100,000-1,000,000 different candidate modulator compounds are possible using the methods of the invention.

The following examples are presented to illustrate the present invention and to assist one of ordinary skill in making and using the same. The examples are not intended in any way to otherwise limit the scope of the invention.

#### EXAMPLE 1

The following provides a general description of how a list of candidate *ceg* sequences was generated. The list was generated by selecting candidate *ceg* gene sequences from a Concordance web engine using the method described in: Brucoleri, R.E., Dougherty, T.J., Davison, D.B. (1998) "Concordance analysis of microbial genomes" in: *Nucleic Acids Res* 26:4482-4486.

#### Microbial Genomics CEG Discovery Process Summary.

##### Microbial Concordance Analysis

The entire genomic sequence data of various bacteria was acquired from several public and proprietary sequence database sources, including GTC (Genome Therapeutics Corporation), and TIGR (The Institute for Genomic Research).

Predicted ORFs from the genomic data were identified, translated, and stored. The desirable ORFs were at least 90 amino acid residues in length. Concordance analysis was performed among bacteria and various parameters were used to filter out genes with high similarity to eukaryotes.

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#### Concordance Analysis

The entire genomic sequence of various Eubacteria was acquired from several public and private sources. The proprietary PathoGenome System from Genome Therapeutics Corporation, Waltham, MA, USA contributed data. Public data was obtained from  
10 GenBank (<http://ncbi.nlm.nih.gov>), The Institute for Genomic Research (TIGR), the Yeast Proteome Database, from Proteome, Inc. of Beverly, MA, and the Sanger Center of the Medical Research Council of the United Kingdom (<http://www.sanger.ac.uk>). Additionally, the non-microbial sequence data used as a basis for comparison and data  
15 subtraction was obtained from a proprietary database, including the LifeSeq Database from Incyte Pharmaceuticals, Palo Alto, CA.

Where required, Incyte nucleotide sequences were translated into protein sequences in all six possible reading frames. GTC supplied predicted protein sequences with their data. In  
20 the case of other eubacterial nucleotide sequences, the program CRITICA (Badger, J. and Olsen, G., 1999 "CRITICA: coding region identification tool invoking comparative analysis" in: *Molecular Biology and Evolution* 16:512-524). The sequences were stored in flat files on a Unix computer system. Each predicted amino acid sequence had to be greater than 90 amino acids.

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Each predicted protein sequence was compared to every other sequence (an "all-against-all" comparison). The program used was FASTA (Pearson, W.R., "Flexible sequence similarity searching with the FASTA3 program package." *Methods in Molecular Biology* 2000 132:185-219.) The parameters used were ktup=2, and all scores above the default  
30 cutoff were kept. The output was processed and stored in a PostGres 95 database (<http://www.postgresql.org>). Graphical user interfaces, using web browser technology, were constructed to query the database.

A Concordance Analysis was performed on the data. The question used to generate the dataset was show all *Streptococcus pneumoniae* open reading frames with a similarity  
5 greater than or equal to 30% overall protein sequence identity to both selected gram-positive and/or gram-negative bacteria in the database. The data was further required not to match yeast or human sequences at greater than 30% overall protein sequence similarity. The resulting dataset included a list of more than 400 conserved amino acid sequences having known or unknown function. The amino acid sequences having  
10 unknown functions formed the basis of a list designated Conserved Unknown Reading Frames, or CURFs which is a subset of the total list of CEGs (e.g., CURFs includes known and unknown).

The resulting list of conserved genes (e.g., more than 400 sequences) was used as a basis  
15 for selecting and screening bacterial gene sequences that are essential for cell viability. The Concordance system was designed to permit high-throughput identification of conserved gene sequences in the database. (Brucoleri, R, Dougherty, T, and Davison, D. 1998 "Concordance analysis of microbial genomes" *Nucleic Acids Res.* 26:4482-4486.)

## 20 Data Curation And Analysis

Exact N-terminal and C-terminal translational start sites of genes were identified by pairwise similarity searches, multiple sequence alignments. Ribosome binding sites, terminators, nearby genes, operons were identified.

25 The resulting list of conserved genes was used as a basis for selecting and screening bacterial gene sequences that are essential for cell viability. This Concordance system was designed to permit high throughput use of the conserved gene sequences contained on the list. A set of Knockout PCR primers were generated, based on the list of  
30 conserved genes, for the purpose of use in the gene disruption procedure described below. The PCR primers were designed to amplify a central 300-500 bp region of the *ceg* (to prevent generation of a functional copy of the *ceg* gene following integration),

ordered electronically, the primers were placed in a 96-well format, and used in the gene disruption procedure as described below.

## EXAMPLE 2

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The following provides a description of the procedure to generate recombinant vectors of pEVP-3 having inserts of candidate *ceg* nucleotide sequences. The Knockout primers generated by the method described in Example 1 above were used to generate DNA fragments comprising candidate *ceg* sequences.

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### Genomic PCR Knockout Target Fragment Generation

96-well plate format were set up (36  $\mu$ l H<sub>2</sub>O, 5  $\mu$ l 10 $\times$  Vent<sup>TM</sup> buffer, 1  $\mu$ l gene specific, knockout forward primer (0.5  $\mu$ g/ $\mu$ l), 1  $\mu$ l gene specific knockout reverse primer (0.5  $\mu$ g/ $\mu$ l), 0.5  $\mu$ l Vent<sup>TM</sup> DNA polymerase (2000 U/ml New England Biolabs, Beverly, MA), 1.5  $\mu$ l each dNTPs (10mM; 6.0  $\mu$ l total), 0.5  $\mu$ l *S. pneumoniae* chromosomal DNA (0.5  $\mu$ g/ $\mu$ l), 50  $\mu$ l total volume/reaction):

15

The nucleotide sequences of the forward and reverse knockout primer pairs were generated from the nucleotide sequence information obtained from the Genomic Therapeutics Corporation database for *Streptococcus pneumoniae*. The primer pairs were each used in a PCR reaction to generate a unique internal (e.g., central region) fragment of the candidate gene targeted for knockout.

20

The PCR program was set in the PCR machine (Initial 95  $^{\circ}$ C - 5 minutes; 30 Cycles of: 95  $^{\circ}$ C - 1 minute, 58  $^{\circ}$ C - 1 minute, 72  $^{\circ}$ C - 30 seconds; Final, 72  $^{\circ}$ C - 10 minutes, 4  $^{\circ}$ C - hold indefinitely). 5  $\mu$ l of each reaction was run on an 0.8% agarose gel after purifying fragment over PCR purification kit (Qiagen) to visualize the fragments then ligation reactions were performed.

25  
30

Ligation Reactions proceeded (set up in 96-well plate format (10.0 µl genomic PCR fragment (generated from step 2 above), 1.0 µl pEPV-3 SmaI-cut vector (1: 10 dilution of vector DNA at 50-100 ng/µl), 1.5 µl 10× ligation buffer (New England Biolabs™), 1.0 µl T4 DNA Ligase (New England Biolabs™ 400,000 U/ml), 1.5 µl ddH<sub>2</sub>O, 15.0 µl total reaction volume).

Reactions were allowed to incubate in 96-well plate at 14 °C overnight in the PCR machine. Transformations into *E. coli* for in vivo amplification were proceeded the following day.

10

The nucleotide sequences of the forward and reverse primer pairs used for the polarity test were generated in a similar manner, from the nucleotide sequence information obtained from the Genomic Therapeutics Corporation database for *Streptococcus pneumoniae*. The primer pairs were each used in a PCR reaction to generate a unique fragment of the candidate gene targeted for the polarity test. The fragment generated for the polarity test included the entire *ceg* coding sequence region but lacking the expression regulatory sequences.

15

Transformation into *E. coli* (strain LE392):

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The next day, 3 µl of above ligation mix was used per transformation reaction plus 50 µl LE392 competent cells. Reactions were set up in 96-well plate format; incubated on ice for 30 minutes; heat-shocked at 42° C for 90 seconds; and incubated on ice 2 minutes; 100 µl SOC media (Gibco BRL) was added; then incubated at 37° C on platform shaker for 1 hour; plated on LB/chloramphenicol (13.0 µg/ml) agar plates for constructs overnight at 37° C with plates inverted and proceeded with colony PCR to confirm constructs. The universal primers flanking the insert site in pEVP-3 were used for PCR amplification.

25

The colony PCR involved the following. 96-well plate format was set up (36.5 µl H<sub>2</sub>O, 0.5 µl pEPV3 forward primer (0.25 µg/µl), 0.5 µl pEPV3 reverse primer (0.25 µg/µl), 1.5

30



µl each (6.0 µl total) dNTPs (10 mM), 0.5 µl Vent™ DNA polymerase, 5 µl 10× Vent™ buffer, 1 µl of a 1:50 cell dilution, 50 µl total volume).

pEPV3 forward primer: 5' CATCAAGCTTATCGATACCGTCG 3' (SEQ ID NO:437)

5 pEPV3 reverse primer: 5' CACAGTAGTTCACCACCTTTTCCC 3' (SEQ ID NO:438)

Colonies of *E. coli* LE392 were picked onto a master plate of LB + 13 µg/ml chloramphenicol (incubate throughout the day at 37° C) and then into 50 µl H<sub>2</sub>O which has been placed into a 96-well plate. 1 µl of this dilution was used in above PCR reaction  
10 (if the 96-well dilution plate is kept you will not need to prepare a master plate). Cultures for minipreps of plasmid candidates may be prepared directly from the cell dilutions.

The PCR program was run (95 °C - 5 minutes, 30 Cycles of: 95 °C - 1 minute, 58 °C - 1 minute, 72 °C - 30 seconds, 72 °C - 10 minutes, 4 °C - hold).

15

A 10 µl/ reaction was run on a 1.0 % TBE gel. A gel designed for 96 well plates and a multichannel pipettor were used to ease loading of the sample rows. The gel was run and stained with ethidium bromide. The positive clones were identified with appropriate molecular size insert(s), amplified by the flanking pEVP-3 primers.

20

#### Minipreps Of Plasmids To Identify Cells Carrying The Pevp-3 Vector With An Insert

The constructs that carried an insert were identified. The constructs having an insert were inoculated into a 5 ml LB/Cm culture, and incubated over night at 37 °C with  
25 aeration. Miniprep plasmid DNA was prepared by a standard procedure. The miniprep DNA was digested with appropriate restriction enzymes to confirm the presence of the insert (enzymes flank SmaI site in pEVP-3) (10 µl miniprep DNA, 2 µl 10 × buffer, 1 µl XbaI, 1 µl XhoI, 6 µl ddH<sub>2</sub>O, 20 µl total volume for digest).

To confirm the presence of an insert, the digest reactions were electrophoresed on an agarose gel and the gel was stained with ethidium bromide. The positive clones were used for the *S. pneumoniae* KNOCKOUTs procedure.

- 5 The confirmatory PCR reactions, using knock out-specific primers (quality control step) involved 35.5  $\mu$ l H<sub>2</sub>O, 5  $\mu$ l 10  $\times$  Vent™ buffer, 1  $\mu$ l knockout forward primer (0.5  $\mu$ g/ $\mu$ l), 1  $\mu$ l knockout reverse primer (0.5  $\mu$ g/ $\mu$ l), 0.5  $\mu$ l Vent™ (6.0  $\mu$ l total) DNA Polymerase (2000 U/ml), 1.5  $\mu$ l each dNTPs (10mM, 6.0  $\mu$ l total), 1.0  $\mu$ l miniprep DNA from test clone, 50  $\mu$ l total reaction volume. The PCR program was as follows: 95 °C for 5  
10 minutes, 30 Cycles of: 95 °C for 1 minute, 60 °C for 1 minute, 72 °C for 30 seconds, 72 °C for 10 minutes, hold at 4 °C. The presence of the correct-sized insert was confirmed by agarose gel electrophoresis and ethidium bromide staining. The confirmed clones were used for the *S. pneumoniae* gene KNOCKOUT procedure. Glycerol stocks were made of all positive *E. coli* LE392 constructs and frozen at - 80 degrees C.

15

### EXAMPLE 3

- The following provides a description of the high throughput gene disruption procedure used in *S. pneumoniae* strain (e.g., gene knockout procedure). The candidate *ceg*  
20 fragments that were generated by the method described in Example 2 were used in the gene disruption procedure in order to identify *ceg* nucleotide sequences that are required for cell viability.

- Reactions were set up in a 1.5 ml eppendorf tubes or 96 well plate (1  $\mu$ g total of miniprep  
25 pEVP-3 + insert DNA (usually 10  $\mu$ l of Qiagen miniprep DNA); then 200  $\mu$ l of *S. pneumoniae* (strain Rx-1) competent cells diluted 1:10 in competence media was added (1 ml of competence media = 980  $\mu$ l Todd Hewitt (Difco Laboratories) with 0.5% yeast extract, 20  $\mu$ l 10% BSA, 1  $\mu$ l 10 % CaCl<sub>2</sub>, and 0.5  $\mu$ l (200  $\mu$ g/ml) Csp-1 competence peptide).

30

Controls were run with each KNOCKOUT experiment and involved 1 µg pEPV3 *Lyt A* construct = positive control (non-essential), or 1 µg pEPV3 *Fts Z* construct = negative control (essential). Then the 96 well plates and controls were incubated at 37 °C for 2.5 to 3 hours in 37 °C room without shaking. The 200 µl of the samples were plated on  
5 Todd Hewitt agar plates with 0.5% yeast extract and 2 µg/ml chloramphenicol.

The samples were incubate over night at 37 °C in 5% CO<sub>2</sub> incubator. Control plates were checked for presence of colonies (pEVP-3::*lytA*) and no growth (pEVP-3::*ftsZ*). Plates were examined for growth (ca. 70-150 colonies) designating nonessentials and zero  
10 colonies designating essential genes.

The polarity test was performed in a similar manner, using the polarity fragments described in Example 3.

15

#### EXAMPLE 4

The following provides a description of the autolysin procedure used to determine that the non-essential control samples of *S pneumoniae* contain a disrupted *lytA* gene.

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#### Phenotypic Autolysin Test

The culture plates containing transformants carrying the *lytA* control vector were flooded  
25 with 0.1% deoxycholate in H<sub>2</sub>O. The plates were observed after 5-10 minutes. Plates with "ghosts" indicated intact *lytA* gene, or plates without "ghosts" indicated a disrupted *lytA* gene. The "ghost" phenomenon is due to detergent triggered autolysis of the cells, causing a gradual fading of the colonies.

30 The detergent treatment triggers the autolysin in *lytA* intact cells; it cannot trigger the autolysin (*lytA* gene product) in *lytA* disrupted cells. Colonies with intact *lytA* "ghost" in 5-10 minutes due to massive pneumococcal cell lysis.

## EXAMPLE 5

The following provides a description of the procedure used to express the CEG proteins  
5 (e.g., designated CFE proteins) in *E. coli* cells.

### CEG Protein Production

Full-length *ceg* gene were inserted into pET-21 expression vector using the *E. coli* BL21  
10  $\lambda$ DE3 expression system using the following method:

For each *ceg*, custom primers were used to insert N- and C- termini into vectors such that  
the 5' end (N-terminus of the CEG) is positioned properly for expression behind the T7  
promoter and optimally placed with regard to the pET ribosome binding site. The pET  
15 vectors contain an *NdeI* site which allows positioning of ATG start site in the vector. In  
cases where the *ceg* sequence contains an internal *NdeI* site, blunt ligation of the *ceg* PCR  
fragment into the vector is accomplished via Klenow fill-in of the *NdeI* site. In many  
cases, primers were also designed such that the *ceg* 3' (C-terminus of the expressed  
protein) will contain an in-frame extension of 6X-histidine residues, encoded in the  
20 vector sequence of pET-21. The individual *cegs* were PCR amplified via custom  
designed primers as described above. Both *ceg* PCR and vector DNA were digested with  
appropriate restriction enzymes. The full-length *ceg* were ligated into the pET  
expression vector. The ligation mixture was transformed into competent *E. coli* BL21  
 $\lambda$ DE3 cells and selected for transformants on LB agar with 50  $\mu$ g/ml ampicillin. Positive  
25 insert bearing clones were screened via minipreps of the plasmids and size analysis on  
0.8% agarose gels, with detection by ethidium bromide staining, as above.

### Protein Production

30 The proper reading frame of each *ceg* inserted into pET-21 is verified by DNA  
sequencing.

A small (2-5 ml) test culture of *E. coli* BL21  $\lambda$ DE3 with the insert-bearing plasmid is tested for protein expression by IPTG induction of the expression vector for 1-2 hours. The expression is verified by SDS-Polyacrylamide Gel Electrophoresis analysis of a whole cell extract (SDS extract of 0.5-1 ml of cells treated at 100 °C for 5 minutes) to determine whether the protein is over-expressed and migrates at the correct predicted molecular weight.

The protein is overproduced and purified via the following method. A large scale (500-1000ml) culture of *E. coli* is grown to early logarithmic phase in broth (e.g., LB broth) and protein expression induced for 2 hours with IPTG (isopropyl-D-thiogalactoside). The cells are harvested by centrifugation (8000 X G; 15 minutes) and the cell pellets resuspended in 20 ml. of buffer. The cells are lysed by sonication, and the supernatant fluid centrifuged at low speed (5000 X G, 15 min.) to remove unbroken cells. The supernatant fluid, containing the over-expressed protein is subjected to Ni-NTA affinity column chromatography (Quiagen, Inc., Chatsworth, CA). The 6X-histidine residues linked at the C-terminal end of the CEG proteins permit rapid protein purification via selective binding to a Ni-NTA resin column. The protein-bound Ni-NTA resin was to remove contaminants, and the bound proteins subsequently eluted with imidazole and recovered. It is possible to upscale this procedure to larger volumes for higher yields of proteins.

#### EXAMPLE 6

The following provides a description of the methods used to purify all 2CEG polypeptides (e.g., 2CFE polypeptides #19-117; SEQ ID NOS:349-436) having a histidine tag at their C-terminal ends. The 2CEG polypeptides having the his-tags were produced by the methods described in Example 5, *supra*. As an example, results of purification of 2CFE 75 polypeptide are presented.

### Production Of The CFE Polypeptides

The BL21 $\lambda$ DE3 cells harboring recombinant pET-21 vectors carrying a 2CFE nucleotide sequence (SEQ ID NOS:244-331) were cultured in LB broth containing ampicillin.

- 5 When the A<sub>600</sub> reached approximately 0.6, protein production was induced by adding 1.0 mM of IPTG, the cells were cultured for an additional 2 hours. The cell pellet was collected by centrifugation, and the collected cell pellet was sonicated in Solution A (50 mM NaPO<sub>4</sub>; 300 mM NaCl, pH 8.0). The sonicated cells were centrifuged at 10,000 RPM to remove the debris.

10

### Purification Of The CFE Polypeptide

- The supernatant was diluted with Solution A, loaded onto a Ni-NTA column (Quiagen) equilibrated with Solution A; the column bed size was 2.5 x 25 cm, and the flow rate was approximately 3.0 ml/minute. The 2CFE protein was eluted using a linear gradient of imidazole, using 0-250 mM in 450 ml, flow rate approximately 3.0 ml/minute. The eluted samples were collected as 22 ml fractions per tube and the eluted samples were monitored using spectrophotometry. The amount of protein in the eluted fractions was estimated using the Bradford method (Bradford, M. M., 1976 *Anal. Biochem.* 72:248) and
- 15 the samples were run on an SDS-PAGE gel (Novex EC6008) (Figure 3 A). Fractions were selected for pooling based on the results of the SDS-PAGE gel. The pooled fractions were concentrated using a 10,000 MW Centricon (Amicon) to approximately 5 ml.

- 25 The 2CFE 75 polypeptide, a precipitate formed and was redissolved upon increasing the sample volume and removing the imidazole by repeated concentration in 50 mM Tris, 100 mM NaCl, pH 7.5. Varying amounts of the 2CFE 75 polypeptide were diluted in either 20 mM Tris, 20 mM KCl, pH 7.5 or 20 mM Tris, 20 mM MgCl<sub>2</sub>, pH 7.5 at concentrations of 12, 24, or 36 ug/ml. The diluted samples were electrophoresed on an
- 30 SDS-PAGE gel under non-reducing conditions (Figure 3 B). The results of Figure 3 B suggests that 2CFE 75 forms a multimer.

**EXAMPLE 7**

The following provides a description of the methods used to purify CEG polypeptides that lack a histidine tag (e.g., 2CFE polypeptides #1-17; SEQ ID NOS:332-348). As an example, the results of purification of CFE 3 polypeptide are presented.

Purification of the CFE 3 Polypeptide

The 2CFE 3 polypeptide was produced using the large scale IPTG-induced method described in Example 5, *supra*. The 2CFE 3 (SEQ ID NO:334) polypeptide lacks a C-terminal histidine tag. The 2CFE 3 polypeptide was purified using a 2-column procedure. The 2CFE 3 polypeptide preparation was eluted from a 26/10 Q Sepharose column (Pharmacia) using a 0-1.0 M NaCl gradient, 2 ml/minute flow rate, and the gradient size was 1 liter. Then the 2CFE 3 polypeptide was eluted from a hydroxyapatite Bio-gel column (Bio-Rad) using a 5-200 mM potassium phosphate (pH 8.0) gradient, the flow rate was 0.3 ml/minute, and the gradient size was 300 ml. A sample of the 2CFE 3 preparation was run on a polyacrylamide gel (Figure 4).

**EXAMPLE 8**

The following provides a description of the size exclusion chromatography methods used to estimate the molecular weight and determine whether the CEG polypeptides oligomerize. The CFE polypeptide may oligomerize to form monomers, dimers, tetramers, hexameric rings, or other oligomeric forms.

Size exclusion chromatography was performed on all isolated 2CFE polypeptides #s 1-117 (e.g., SEQ ID NOS:332-436). This method was performed using various types of columns, depending on the particular 2CFE polypeptide tested.

The Biosil SEC-125 HPLC Gel Filtration column (BioRad Laboratories, Inc) was used, for example, to characterize CFE 8. The mobile phase was 0.2 M  $\text{KH}_2\text{PO}_4$ , 0.9% NaCl pH 6.8.

- 5 The Phenomenex 600 x 7.5 mm Biosep SECS 3000 column was used, for example to characterize 2CFE 21 and 39. The mobile phase for size exclusion was 50 mM  $\text{Na}_2\text{HPO}_4$ , pH 7.0 and 150 mM NaCl run at 1 ml/minute in a Gilson HPLC system, with protein detection at 280 nm.

## 10 EXAMPLE 9

The following provides a description of the computer-aided methods used to search for similarities between the amino acid sequences of the CEG polypeptides and sequences available through public and proprietary databases. In many cases, the function of the CEG polypeptides was suggested by the results of the similarity searches. The function of some of these CEG polypeptides has been confirmed by performing additional analyses. Table V provides a list of the suggested and confirmed functions of CEG polypeptides designated CFEs #1-117.

- 20 The putative function of the CFE polypeptides were determined using computer-aided bioinformatic approaches, including distant homologies, motif searching, or predictions based on statistical rules. For example, the distant homology approach involved pairwise or multiple sequence alignments, employing tools such as FASTA, and Psi-BLAST. The motif searching approach involved using sophisticated hidden Markov models. The approach based upon predictions of statistical rules involved prediction of transmembrane regions, coiled-coil, and other structural motifs. These approaches have been reviewed in *Computational Methods In Molecular Biology* 1998, eds. Salxber, S.L., Searls, D.B. Searls, and Kasif, S., Elsevier, and in *Bioinformatics: A Practical Guide To The Analysis Of Genes And Proteins* 1998 eds Baxevanis, A. D. and Francis Ouellete, B.F., Wiley-Interscience.

30



- Global sequence similarity searches were performed using the amino acid sequences of all the conserved essential gene sequences (e.g., CFEs 1-117; SEQ ID NOS:114-226) to search against a non-redundant protein database using the BLAST2 algorithm (Altschul S.F., et al., 1997 *Nucleic Acids Res.* 25(17):3389-3402). In a similar search, similar
- 5 sequences were identified in the Concordance database using the "Neighbor" function (Brucoleri R. E., Dougherty T.J., Davison D.B. 1998 *Nucleic Acids Res.* 26(19):4482-4486). To determine if the predicted amino acid sequences were full length and in the proper reading frame, BLAST-type searching and CLUSTAL multiple sequence alignments (Higgins D.G., et al., 1996 *Methods Enzymol.* 266:383-402) were used.
- 10 Local sequence similarity searches were performed, by searching for Prosite (Hofmann K., et al., 1999 *Nucleic Acids Res.* 27(1):215-219) and Pfam motifs (Bateman A., et al., 2000 *Nucleic Acids Res.* 28(1):263-266). Additionally, the amino acid sequences of the CFEs were analyzed by performing protein threading analyses using the ProCeryon fold recognition program (Sippl, et al., 1992 *Proteins* 13:258-271; Sippl, J. 1993 *J. Comp.*
- 15 *Aided Mol. Design* 7:473-501; www.proceryon.com) and Geneformatics.

In bacteria, many operons include genes encoding different proteins that catalyze discrete steps of a common biochemical pathway. Therefore, the operon structures in *S. pneumoniae* was compared with that in other bacteria in order to predict the function of

20 CFE polypeptides.

Additionally, analysis of bacterial metabolic pathways were performed using Pathway Tools from DoubleTwist, based on the EcoCyc system (Karp P.D., et al., 1999 *Nucleic Acids Res.* 1999 27(1):55-58). This analysis was used to predict which CFEs mediate

25 various steps of the pathways.

When the sequence identity between a CFE polypeptide and the annotated database (e.g., SwissProt, Genbank) was low (e.g., sequence identity less than about 30%), a Protein Threading (e.g., fold recognition) method was used to predict similarities in the folded

30 protein structure of CFE polypeptides in the absence of a high level of sequence similarity with proteins in the databases (review by Teichmann, et al., 1999 *Current Opinion in*

*Structural Biology* 9:390-399). The Protein Threading method predicts the compatibility of a query sequence (e.g., CFE polypeptide sequences) with each of the folds in a library of known protein structures. The library of known protein structures as developed, maintained, and updated throughout the search process.

5

A list of potential structural folds, onto which each query was compatible, was generated for all CFE polypeptides (e.g., SEQ ID NOS:114-226). The fold assignments for each query were used to generate pairwise sequence alignments. The pairwise sequence alignments were used to generate protein models of the query polypeptide (e.g., CFE polypeptides).

10

The pairwise sequence alignments were also used to compare the position of critical residues of the structural template with the query polypeptide. The list of critical residues was generated by using multiple sequence alignments derived from a structural classification of proteins to generate a conservation profile which provided sequence-specific positions conserved across a homologous family of protein folds. Comparative modeling was used to search the model of the query polypeptide for the critical residues and determine whether the structural and functional motifs are conserved in the query protein. Conservation of structural and functional motifs permitted assignment of putative structure and function to a query polypeptide sequence.

15

The Protein Threading method was used to search for putative folded structure and function for all CFE polypeptides (SEQ ID NOS:114-226). The CFE polypeptides having significant sequence identity (e.g., more than 30%) to known proteins were assigned putative functions with a high level of confidence.

20

#### EXAMPLE 10

The following provides a description of the methods used to characterize purified, CFE 101 polypeptide. The 2CFE 101 polypeptide mediates the conversion of pantothenate to 4' phosphopantothenate, and is predicted to be a pantothenate kinase.

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### Computer-Aided Comparison

The computer-aided comparison, as described in Example 9 *supra*, suggests that the amino acid sequence of the CFE 101 polypeptide (SEQ ID NO:210) is 42% similar to the amino acid sequence of the *coaA* protein of *E. coli*. Thus, CFE 101 may be a pantothenate kinase, which mediates the conversion of pantothenate to 4' phosphopantothenate (Figure 5).

### Circular Dichroism and Circular Dichroism Thermal Melt Analysis

Circular dichroism and circular dichroism melt methods were used to determine the folded structure of the expressed and isolated 2CFE polypeptides. For example, this method was used to characterize the folded structure of isolated 2CFE 101 (SEQ ID NO:421).

The starting concentration of the 2CFE 101 polypeptide was such that OD<sub>205</sub> was approximately 1.5, and the OD<sub>280</sub> was approximately 0.05 (e.g., 0.05 to 0.1 mg/ml). The starting concentration of 2CFE 101 was approximately 344  $\mu$ M in 50% glycerol, 50 mM Tris, 100 mM NaCl, 5 mM MgCl<sub>2</sub>, 0.5 mM EDTA, at pH 7.5. The polypeptide was diluted to a final concentration of 7  $\mu$ M, as determined by absorbance at A<sub>280</sub>, in 20 mM Na-phosphate, 100 mM KCl, at pH 7.0. The circular dichroism analysis was performed using quartz cuvettes, the instrumentation was from JASCO (Model J-720), the readings were performed at 25 degrees C (Figure 6 A). The band width was 1 nm, the sensitivity was 20 mdeg, the response was 0.25 seconds, the scan speed was 50 nm/minute, and the step was 0.5. The circular dichroism thermal melt analysis was performed at a range of between 0 and 100 degrees C (Figure 6 B). Additionally, the circular dichroism was performed comparing monomer and aggregate pools of 2CFE 101.

### Size Exclusion Analyses

Size exclusion chromatography methods were performed using the Biosil SEC column, as described in Example 8 *supra*. The results suggest that the 2CFE 101 polypeptide  
5 forms monomer (40,200 Da) and oligomers (194,000 Da). The specific activity of the monomer and oligomeric forms of 2CFE 101 were determined, as described below.

### Biochemical Assays

10 The biochemical assays of the 2CFE 101 polypeptide was based on the PK/LDH coupled enzyme assays described by Vallari, D. S., et al. (1987 *J. Biol. Chem.* 262:2468-2471) and Song, W. -J., et al., (1994 *J. Biol. Chem.* 269:27051-27058).

Briefly, the assay was performed as follows. The reaction included: 885  $\mu$ l of 0.1 M  
15 Tris-HCl (pH 7.6), 25  $\mu$ l NADH (14.1 mM), 20  $\mu$ l ATP (10.7 mM), 50  $\mu$ l phospho-enol-pyruvate (56 mM), 5  $\mu$ l LDH/PK (lactose dehydrogenase/PK; Sigma, catalog # P-0294, 60 U/ ml PK, 1050 U/ml LDH), 5  $\mu$ l of the 2CFE 101 polypeptide (9 mg/ml in 50 mM Tris-HCl, pH 7.5, 100 mM NaCl which was diluted to 4.5 mg/ml in 50% glycerol). The reaction was started by adding 10  $\mu$ l pantothenate (100 mM; Sigma, catalog # P2250).  
20 The production of ADP in the reaction was monitored by measuring the absorbance at 340 nm. The results in Figure 8 show that the 2CFE 101 polypeptide mediates ADP production in the presence of pantothenate and ATP. The  $K_m$  of pantothenate ( $n=4$ ) was  $144 (\pm 16.5) \mu$ M, the  $V_{max}$  of the 2CFE 101 polypeptide ( $n=4$ ) was  $2.04 (\pm 0.25) \mu$ M  $\text{min}^{-1} \text{mg}^{-1}$ . The monomer form has a specific activity of approximately  $1.7 \mu$ M  $\text{min}^{-1} \text{mg}^{-1}$ .  
25 The oligomeric form has a specific activity of  $0.26 \mu$ M  $\text{min}^{-1} \text{mg}^{-1}$ .

Alternatively, the 2CFE 101 polypeptide can be tested in an assay that monitors the conversion of pantothenate to 4'-phosphopantothenate. The same reaction described above can be used, except  $^{14}\text{C}$ -labeled pantothenate is used. The reaction can be  
30 monitored by measuring the amount of  $^{14}\text{C}$ -labeled 4'-phosphopantothenate produced.

**EXAMPLE 11**

The following provides a description of the methods used to characterize purified, CFE 39 and CFE 21 polypeptides, carrying a C-terminal histidine 6-tag. The methods include  
5 helicase reactions, in which synthetic Holliday Junction templates are resolved into duplex structures. In one method, helicase reaction was monitored using radiolabeled templates. In another method, the helicase assay was adapted for use in a high throughput assay employing fluorescence labeled templates.

**10    Computer-Aided Comparison**

The computer-aided comparison, as described in Example 9 *supra*, suggests that the CFE 39 polypeptide (SEQ ID NO: 148) is an RuvA homologue. The comparison also suggests that CFE 21 (SEQ ID NO:132) is an RuvB homologue.

15

Previous studies by Parsons and others have shown that RuvA and RuvB proteins, in *E. coli*, promote branch migration or movement of Holliday Junctions during genetic recombination and DNA repair (Parsons, C. A., et al., 1992 *Proc. Natl., Acad. Sci. USA* 89:5452-5456; Tsaneva, I. R., et al., 1993 *Proc. Natl., Acad. Sci. USA* 90:1315-1319;  
20 Muller, B., et al., 1993 *J. Biol. Chem.* 268:17179-17184; Mitchell, A. H. and S. C. West 1996 *J. Biol. Chem.* 271:19497-19502; Parsons, C. A. and S. C. West 1993 *J. Molec. Biol.* 232:397-405; Tsaneva, I. R., et al., 1992 *Molec. Gen. Genet.* 235:1-10; Mitchell, A. H. and S. C. West 1994 *J. Molec. Biol.* 1994 243:208-215).

**25    Size Exclusion Chromatography**

Size exclusion chromatography was performed on 2CFE 39 (SEQ ID NO:366) and 2CFE 21 (SEQ ID NO:350) using the Phenomenex 600 x 7.5 mm Biosep SECS 3000 column, as described in Example 8 *supra*. Protein standards (BioRad) were used to calibrate the  
30 column, including thyroglobulin (670,000 Da), gamma globulin (158,000 Da), ovalbumin (44,00 Da), myoglobin (17,00 Da), and B-12 (1350 Da).

The results indicate that 2CFE 39 (RuvA) forms tetramers and 2CFE 21 (RuvB) forms a hexameric ring structure. Selected eluted samples were electrophoresed on a polyacrylamide gel (Novagen) (Figure 9).

5

#### The Holliday Junction Analysis Using Radiolabeled Templates

The Holliday Junction analysis was performed using radiolabeled, synthetic, asymmetrical, Holliday Junction templates, as described in Hiom, K. and S. C. West  
10 1995 *Cell* 80:787-793. The Holliday Junction templates were produced by annealing together four separate, single-stranded, oligonucleotide strands to form four-stranded structures (e.g., the Holliday Junction template). The Holliday Junction templates were reacted with the 2CFE 39 and 2CFE 21 polypeptides, in a helicase reaction, to test their ability to generate two duplex structures.

15

#### Producing the Synthetic Holliday Junction Templates

The asymmetrical Holliday Junction templates were produced by annealing the following oligonucleotide sequences:

20

Oligonucleotide strand 1:

5'-CCAGTGATCACATACGCTTTGCTAGGACATCTTGATATCAGCCCACGTT  
CACCCGCCTACCAGTGCCACGTTGTATGCCACGTTGACC-3' (SEQ ID NO:438)

25 Oligonucleotide strand 2:

5'-GGGTCAACGTGGGCATACAACGTGGCACTGGTAGGCGGGTGAACGTGGG  
CTGATATCAAGATGTCCATCTGTCCGTTCTATGACGT-3' (SEQ ID NO:439)

Oligonucleotide strand 3:

30 5'-AACGTCATAGATGAACGGACAGATCATGGTGCTTTTAAAGTCTAGAGAC  
TATCGAGCATTAGTACCAGTATCGAATCCGTCTTGTC-3' (SEQ ID NO:440)

Oligonucleotide strand 4:

5'-TTTGACAAGACGGATTCGATACTGGTACTAATGCTCGATAGTCTCTAGAC  
TTTAAAAGCACCATGTAGCAAAGCGTATGTGATCACTG-3' (SEQ ID NO:441)

5

Oligonucleotide strand 3 was labeled at the 5' end using approximately 300 ng of oligonucleotide strand 3, 1  $\mu$ l 10x Phosphate Buffer, 5  $\mu$ l  $^{32}$ P ATP, 1  $\mu$ l T4 polynucleotide kinase (Gibco-BRL)), in a 10  $\mu$ l volume, and the reaction was performed at 37 degrees C for 30 minutes. The reaction was loaded onto a G50 column to remove the  
10 unincorporated radiolabel. The final concentration of the radiolabeled oligonucleotide strand 3 was approximately 15 ng per  $\mu$ l.

Approximately equimolar amounts of the four oligonucleotide strands were annealed (e.g., hybridized). The annealing reaction included: 5  $\mu$ l Annealing Buffer (200 mM  
15 Tris-Cl pH 8.0, 100 mM MgCl<sub>2</sub>, 1 M NaCl, 10 mM DTT); 450 ng of radiolabeled oligonucleotide strand 3; and 1000 ng each of oligonucleotide strands 1, 2, and 4; in 50  $\mu$ l total reaction volume. The control annealing reaction included: 5  $\mu$ l Annealing Buffer, 60 ng radiolabeled oligonucleotide strand 3; 1000 ng oligonucleotide strand 4; in 50  $\mu$ l total reaction volume. Annealing was performed at 95 degrees C for 5 minutes, 65  
20 degrees C for 30 minutes, 42 degrees C for 30 minutes, and room temperature (e.g., between about 23 to 27 degrees C) for 30 minutes to generate the synthetic Holliday Junction templates. The synthetic Holliday Junction templates were gel or column-purified to remove the duplex and non-annealed products. As a control, oligonucleotide strands 3 and 4 were annealed to form duplex structures. The synthetic Holliday Junction  
25 templates and duplex structures were stored at -20 degrees C.

#### CFE 39 and CFE 21: The Helicase Reaction Using Radiolabeled Templates

The helicase reaction was performed to determine whether 2CFE 39 and 2CFE 21  
30 resolved the synthetic Holliday Junction templates into duplex structures. The helicase reaction was performed as follows. A 50  $\mu$ l total reaction volume included: 25  $\mu$ l of 2x

Reaction Buffer (50 mM Tris-Cl pH8.0, 30 mM MgCl<sub>2</sub>, 2 mM ATP); 1 µl synthetic Holliday Junction template (36 ng); 2 µl 2CFE 39 (1 µM); and 2 µl 2CFE 21 (1 µM). The reaction was incubated at 37 degrees for 30 minutes. The reaction was stopped by adding 5 µl Stop Buffer (100 mM Tris-Cl pH 7.5, 5 mg/ml Proteinase-K, 5% SDS). The  
5 stopped reaction was returned to 37 degrees C for 5 minutes. The helicase reaction was loaded onto and run on a non-denaturing, 12% PAGE, Tris-glycine gel.

The results shown in Figure 10, lanes 6, 7 and 8, indicate that the 2CFE 39 and 2CFE 21 polypeptides resolved the synthetic Holliday Junction templates into duplex structures.

10

#### CFE 39: The Helicase Reaction

It has been previously shown that *E. coli* RuvA binds to Holliday Junction templates (Parsons, C. A., et al., 1992 *Proc. Natl. Acad. Sci. USA* 89:5452-5456). The ability of *S.*  
15 *pneumoniae* CFE 39 to bind to a Holliday Junction template can be tested by employing the helicase assay described herein. The results of the helicase assay can be monitored by performing a gel shift assay and/or capillary electrophoresis. The presence of a Holliday Junction template bound to 2CFE 39, which migrates more slowly than the Holliday Junction template alone, would indicate that *S. pneumoniae* 2CFE 39 binds to Holliday  
20 Junction templates.

#### CFE 39 and CFE 21: Holliday Junction Analysis Using Fluorescent-Labeled Templates

The helicase reaction described herein was performed using Holliday Junction templates  
25 having one oligonucleotide strand labeled with a fluorescent agent and another strand labeled with a quenching agent. The 5' fluorescent end and the 3' quenching end of the strands that make up the Holliday Junction templates are in proximity to each other, resulting in a non-fluorescent template. When the Holliday Junction templates are resolved into duplex structures, the fluorescent and quench ends are not in proximity to  
30 each other, resulting in fluorescence.



The Holliday Junction templates used to perform this experiment comprised the following: the 5' end of oligonucleotide strand 1 was labeled with a fluorescein (e.g., the fluorescent agent), and the 3' end of oligonucleotide strand 4 was labeled with DABCYL (e.g., the quenching agent). The oligonucleotide strand 1 labeled with fluorescein and the  
5 oligonucleotide strand 4 labeled with DABCYL were custom synthesized (Gibco-BRL Life Technologies, Inc.).

The fluorescein and DABCYL labeled oligonucleotides were annealed in a reaction, as described above, to generate synthetic Holliday Junction templates. The helicase reaction  
10 was performed as described above. The results of the helicase reaction were monitored by measuring the unquenching of the Holliday Junction templates with time (Figure 11).

The helicase assay using Holliday Junction templates labeled with fluorescent-quenching agents can be adapted for use in high throughput analyses to test 2CFE 39, 2CFE 21, and  
15 other polypeptides for their ability to resolve the templates into duplex structures.

## EXAMPLE 12

The following provides a description of the methods used to characterize purified, CFE 8  
20 polypeptide, which lacks a histidine tag. The CFE 8 is a putative DNA single-stranded binding protein.

### Computer-Aided Comparison

25 The computer-aided comparison, as described in Example 9 *supra*, suggests that the CFE 8 polypeptide (SEQ ID NO:121) may be a single stand binding protein homologue, such as SSB.

### Size Exclusion Chromatography

The 2CFE 8 polypeptide (SEQ ID NO:339) was characterized by size exclusion chromatography, using the Biosil SEC-125 HPLC Gel Filtration column as described in Example 8 *supra*. The chromatogram showed one peak corresponding to a molecular weight of approximately 89 kDa. Based on the nucleotide sequence, the predicted molecular weight of 2CFE 8 is 17,351 Da. In non-denaturing conditions, 2CFE 8 forms a multimer.

### 10 Binding Reaction

The 2CFE 8 polypeptide was reacted with a single-stranded oligonucleotide A. Briefly, the binding reaction included: 50  $\mu$ M of 2CFE 8 polypeptide, 50  $\mu$ M oligo strand A, 20 mM Tris/20 mM KCl pH 7.5. The binding reaction was performed at 37 degrees C, for 2 hours.

Oligonucleotide strand A:

5'-TTAGGGCCCGGGCTATCTTACAATCTCGTT-3' (SEQ ID NO:442)

### 20 Capillary Electrophoresis

The results of the binding reaction was monitored by capillary electrophoresis, following the methods described in "Handbook of Capillary Electrophoresis" 2<sup>nd</sup> Edition, 1997, ed. J. Landers.

25

Separation was performed using an uncoated capillary tube (360  $\mu$ m o.d., 50  $\mu$ m i.d., with a 50 cm effective separation length; Watrex International, Inc., Pittsford, NY) and 50 mM borate pH 9.3 as the mobile phase, at 25 kVolts, 20 minutes separation time.

30 The results indicate that 2CFE 8 alone elutes as a sharp peak, indicating little adsorption to the uncoated capillary wall (Figure 12 A). The shape of the peak and peak retention

time changed with 2CFE 8 in the presence of all oligonucleotides tested (Figure 12 B). As a negative control, MurB polypeptide (Pucci, M. J., L. F. Discotto, and T. J. Dougherty 1992 "Cloning and Identification of the Escherichia coli murB DNA sequence, which encodes UDP-N-acetylenolpyruvoylglucosamine reductase" *J. Bacteriol.* 174:1690-1693) was reacted with the same oligonucleotides. MurB reacted with or without the oligonucleotides showed no change in peak shape or retention time.

After capillary electrophoresis analyses, the 2CFE8 alone and 2CFE plus oligonucleotide samples were run on native polyacrylamide gels to determine whether the polypeptide was intact. The results indicate that in all cases, 2CFE 8 was intact and had not degraded with time or storage.

#### Mobility Shift Assays

The ability of 2CFE 8 polypeptide to bind oligonucleotide strand A was tested in a mobility shift assay.

The results indicate that 2CFE 8 binds single stranded oligonucleotides (Figure 13 A and B). In Figure 13 A, the gel was stained with ethidium bromide. The unbound oligonucleotides appear near the bottom of the gel, while the bound oligonucleotides appear near the middle. The same gel was stained with Coomassie (Figure 13 B), revealing that 2CFE 8 polypeptide bound to the oligonucleotide migrated further than unbound 2CFE 8, due to the change in charge carried by the oligonucleotide. Various ratios of 2CFE8:oligo were tested. The optimal binding ratio was 2:1.

#### The Effect of MgCl<sub>2</sub>

The 2CFE 8 polypeptide precipitated in the presence of 5 mM MgCl<sub>2</sub>. The precipitation was reversible by the addition of 1  $\mu$ M of the oligonucleotides tested. The observation indicates specific binding between 2CFE 8 polypeptide and the oligonucleotides tested.

### Scintillation Proximity Assay

Scintillation proximity assay (SPA) methods can be used in a high throughput screening procedure to monitor, for example, a binding reaction. SPA utilizes beads (Amersham) which are coated on the surface with a particular compound or molecule. For example, the SPA bead may be coated with avidin to facilitate binding with any molecule having a biotin tag.

The binding reaction of the 2CFE 8 polypeptide and the oligonucleotide strand A can be monitored using SPA beads and a scintillation counter. The beads can be coated with avidin, the 2CFE 8 polypeptide can be tagged with biotin, and the oligonucleotide strand A can be radiolabeled.

### **EXAMPLE 13**

The following provides a description of the methods used to characterize purified, 2CFE 3 (SEQ ID NO:334) and 2CFE 86 (SEQ ID NO:409) polypeptides.

The 2CFE 3 polypeptide catalyzes the conversion of D-glucosamine-6-phosphate to D-glucosamine-1-phosphate, indicating that 2CFE 3 mediates amino-sugar biosynthesis through the N-acetyl glucosamine pathway (Figure 14).

The 2CFE 86 polypeptide catalyzes the conversion of D-glucosamine-1-phosphate to N-acetylglucosamine-1-phosphate, and the conversion of N-acetylglucosamine-1-phosphate to UDP-N-acetylglucosamine-1-phosphate, which indicates that 2CFE 86 also mediates amino-sugar biosynthesis through the N-acetyl glucosamine pathway (Figure 14).

### Computer-Aided Comparisons Of CFE 3

The computer-aided comparison, as described in Example 9 *supra*, suggested that the CFE 3 polypeptide (SEQ ID NO:116) is a phosphoglucosamine mutase, such as GlmM.

### Purification of the CFE 3 Polypeptide

The 2CFE 3 polypeptide was produced using the large scale IPTG-induced method described in Example 5, *supra*. The 2CFE 3 polypeptide lacks a C-terminal histidine tag.

- 5 The 2CFE 3 polypeptide was purified using a 2-column procedure. The 2CFE 3 polypeptide preparation was eluted from a 26/10 Q Sepharose column (Pharmacia) using a 0-1.0 M NaCl gradient, 2 ml/minute flow rate, and the gradient size was 1 liter. Then the 2CFE 3 polypeptide was eluted from a hydroxyapatite Bio-gel column (Bio-Rad) using a 5-200 mM potassium phosphate (pH 8.0) gradient, the flow rate was 0.3  
10 ml/minute, and the gradient size was 300 ml. A sample of the 2CFE 3 preparation was electrophoresed on an SDS polyacrylamide gel (Figure 4).

### Affinity Capillary Electrophoresis of CFE 3

- 15 Affinity capillary electrophoresis methods were used to determine whether the 2CFE 3 polypeptide binds to various glucose derivatives. Binding was performed under equilibrium conditions, in which the sugars were dissolved in the running buffer and reacts with 2CFE 3 during separation in the column. The affinity capillary electrophoresis method used to analyze 2CFE 3 follows the methods described in  
20 "Handbook of Capillary Electrophoresis" 2<sup>nd</sup> Edition, 1997, ed. J. Landers.

- Briefly, 2CFE 3 polypeptide was reacted with increasing amounts of various glucose derivatives (e.g., substrate) at 25, 30 and 37 degrees C. The glucose derivatives included UDP-glucose, glucose-1-phosphate, glucose-6-phosphate, glucosamine-1-phosphate, and  
25 glucosamine-6-phosphate. The reaction included: 2CFE 3 polypeptide (2.0 mg/ml), separation buffer (25 mM Tris; 192 mM Glycine, pH 8.0; BupH Tris-Glycine Buffer Packs, Pierce). Separation was performed at 25 kVolts, separation time was 15 or 20 minutes.

- 30 The results shown in Figure 15 A indicate that at 25 degrees C, 2CFE 3 binds to D-glucose-1-phosphate in a dose-dependent manner, as the peak shape and/or the retention

time for 2CFE 3 changes in the presence of 100 and 500  $\mu$ M D-glucose-1-phosphate compared to unreacted 2CFE 3.

5 The results shown in Figure 15 B indicate that at 25 degrees C, 2CFE 3 binds to D-glucosamine-6-phosphate in a dose-dependent manner, as the peak shape and/or the retention time for 2CFE 3 changes in the presence of 100 and 500  $\mu$ M D-glucosamine-6-phosphate compared to unreacted 2CFE 3.

10 The results shown in Figure 15 C indicate that at 25 degrees C, the 2CFE 3 polypeptide also binds to glucose-6-phosphate.

A comparison of 2CFE 3 reacted with various glucose derivatives, at 30 degrees C, is shown in Figure 15 D. The results indicate that D-glucosamine-6-phosphate is a putative substrate for 2CFE 3, as this reaction exhibits the greatest change in peak shape and/or retention time.

#### CFE 3: Capillary Electrophoresis and Laser-Induced Fluorescence

20 In a further analysis of 2CFE 3 polypeptide, capillary electrophoresis was performed with laser-induced fluorescence in order to separate and detect interaction between the substrate (e.g., D-glucosamine-6-phosphate) and the product (e.g., D-glucosamine-1-phosphate) in a one dose, one time-point procedure.

25 The 2CFE 3 polypeptide was derivitized by reacting 10 mM FITC (fluorescein isothiocyanate dissolved in methanol; Calbiochem, San Diego, CA) with D-glucosamine-6-phosphate, at ambient temperature, in the dark, overnight. The FITC-derivatized 2CFE 3 polypeptide (2.0 mg/ml) was reacted with the substrate (D-glucosamine-6-phosphate and D-glucosamine-1-phosphate) for one hour.

30 Separation was performed using an uncoated capillary (360  $\mu$ m o.d., 50  $\mu$ m i.d., with a 50 cm effective separation length) and 50 mM borate (pH 9.3) as the mobile phase. The

argon-ion laser had an excitation wavelength of 488 nm and an emission filter of 520 nm (Beckman, Fullerton, CA). The results shown in Figure 16 indicate that 2CFE 3 binds and catalyzes the conversion of D-glucosamine-6-phosphate to D-glucosamine-1-phosphate.

5

#### Computer-Aided Comparison Of CFE 86

The comparison results, as described in Example 9 *supra*, suggested that the CFE 86 polypeptide (SEQ ID NO:195) is an acetyltransferase, such as GlmU which is a bifunctional enzyme in *E. coli*. It has been previously shown that, in *E. coli*, GlmU is a bifunctional protein having both the acetyltransferase and uridylyltransferase active sites (Mengin-Lecreulx, D. and J. van Heijennort 1994 *J. Bacteriol.* 176:5788-5795; Gehring, Al., et al., 1996 *Biochemistry* 35:579-585). The bifunctional enzyme catalyzes the conversion of D-glucosamine-1-phosphate to N-acetylglucosamine-1-phosphate (acetyltransferase), and catalyzes the conversion of N-acetylglucosamine-1-phosphate to UDP-N-acetylglucosamine-1-phosphate (uridylyltransferase). The  $K_m$  of the acetyltransferase and uridylyltransferase reactions has been previously calculated (Mengin-Lecreulx, D. and J. van Heijennort 1994 *supra*). Additionally, the crystal structure of GlmU from *E. coli* is known (Brown, K., et al., 1999 *EMBO J.* 18:4096-4107).

20

#### Purification of the CFE 86 Polypeptide

The 2CFE 86 polypeptide (SEQ ID NO:409) has a C-terminal histidine tag. The 2CFE 86 polypeptide was produced using the large scale IPTG-induced method described in Example 5, *supra*. The 2CFE 86 polypeptide was purified using the Ni-NTA affinity column method described in Example 6, *supra*. The eluted 2CFE 86 polypeptide was dialyzed against 50 mM Tris-Cl, 100 mM NaCl, 25% glycerol, pH 8.0. Samples of the purified 2CFE 86 polypeptide were electrophoresed on a polyacrylamide gel (Figure 17).

30

Coupling CFE 3 and CFE 86 to Produce UDPAG

A biochemical assay was performed, to determine whether 2CFE 3 and 2CFE 86 convert D-glucosamine-6-phosphate to UDP-N-acetylglucosamine-1-phosphate (e.g., UDPAG).

- 5 The 2CFE 3 and 2CFE 86 polypeptides were used in a coupled reaction based on the assays described in Jolly, L. P., et al., 1999 *Eur. J. Biochem.* 262:202-210.

- A time-dependent and dose-dependent assay were performed. Briefly, the assay was performed in 96-well plates, each well including 100  $\mu$ l volume. The assay included: 1  
10 mM D-glucosamine-6-phosphate (Sigma); 0.7 mM D-glucosamine-1,6-diphosphate (Sigma); 1.2 mM acetyl-Coenzyme A (Sigma); and 5 mM uridine-5'-phosphate (Sigma); 3 mM  $MgCl_2$  (Sigma); 50 mM Tris-Cl, pH 8.0 (Life Technologies). The reaction was started by adding 1  $\mu$ g of 2CFE 3; and 10  $\mu$ g of 2CFE 86. The reaction was performed at room temperature. The reaction was stopped at 0, 15, 30, and 65 minutes, by filtering out  
15 the 2CFE polypeptides.

- The results of the assay was monitored by HPLC (high pressure liquid chromatography) using an Optisil 10 $\mu$  SAX column (250 x 4.6 mm), measuring at 262 nm, the mobile phase was 150 mM  $KH_2PO_4$  (pH 3.5), and 1.5 ml/minute flow rate. The results shown in  
20 Figure 18 show the time-dependent assay and indicate that HPLC detected the presence of UDPAG.

CFE 86: The Uridyltransferase Reaction

- 25 The 2CFE 86 polypeptide was tested in a uridyltransferase reaction, in which N-acetyl-D-glucosamine-1-phosphate and UTP produce UDP-N-acetylglucosamine. The uridyltransferase reaction was monitored using a malachite green/inorganic pyrophosphatase assay (e.g., malachite green-IPPAse assay) and/or monitored using HPLC. The malachite green-IPPAse assay was used to measure orthophosphate  
30 production from digestion of the pyrophosphate liberated in the uridyltransferase reaction.



The malachite green reagent was prepared as follows. A 0.045 % solution of malachite green (Sigma; M9636) was prepared in water. A 4.2 % solution of ammonium molybdate (Mallinckrodt) was prepared in 4N HCl. The malachite green and ammonium molybdate were mixed in a 3:1 ratio, and stirred for about 20 minutes. The mixture was filtered, and stored at 4 degrees C. The inorganic pyrophosphatase (Sigma; I-2267) was diluted to 0.1 U/ $\mu$ l in 50 mM Tris/3mM MgCl<sub>2</sub> pH 8.0, and stored at 4 degrees C.

The uridylyltransferase reaction was performed in 96-well plates. The coupled reaction described herein was performed, in the presence of 2CFE 3 alone or 2CFE 3 and 2CFE 86, and included the addition of 0.5 U/well of the diluted inorganic pyrophosphate. The reaction was mixed for 5 minutes at room temperature. The reaction was stopped by the addition of 240  $\mu$ l/well of the malachite green reagent and 30  $\mu$ l/well of 34% sodium citrate, and the reaction was mixed. The results of the uridylyltransferase reaction was monitored by spectrophotometry at 660 nm.

The results of separate uridylyltransferase reactions were monitored by HPLC, using a Phenosphere-NEXT C18 column (250 x 4.6 mm). The mobile phases included A and B as follows: A) methanol/10 mM potassium phosphate pH 6.5 (0:100); and B) methanol/10 mM potassium phosphate pH 6.5 (40:60). The mobile phases were run under the following conditions: 100% mobile phase A for 5 minutes, to 100% mobile phase B in 3 minutes; and hold 100% mobile phase B for 9 minutes. The retention time for the UDPAG product is approximately 5.75 to 6.0 minutes.

The results three uridylyltransferase reactions, monitored by HPLC are summarized in Table III below.

**TABLE III**

<u>Purified CFE 86:</u>	<u>Specific Activity (nmol/min/<math>\mu</math>g):</u>
2CFE 86-1	3.1
2CFE 86-2	3.4
2CFE 86-3	3.1

5

The results of the uridylyltransferase reactions, monitored by HPLC or HPLC and Malachite Green IPPase assays are summarized in Table IV below.

10

**TABLE IV**

<u>Reaction:</u>	<u>K<sub>m</sub> (<math>\mu</math>M):</u>	<u>Method:</u>
<u>Acetyltransferase reaction:</u>		
Glucosamine-1-P	94	HPLC
Acetyl-coA	150	HPLC
<u>Uridylyltransferase reaction:</u>		
N-acetylglucosamine-1-P	48	HPLC and MG/IPPase
UTP	79	HPLC

**EXAMPLE 14**

15

The following provides a description of the methods used to characterize various 2CFE polypeptides, including CFE 21, 34, 35, 39, and 90. The molecular weight of these 2CFE polypeptides were analyzed by size exclusion chromatography and gel electrophoresis. The 2CFE 34, 35, and 90 polypeptides putatively mediate fatty acid biosynthesis.

20

### Computer-Aided Comparison

The computer-aided comparison, as described in Example 9 *supra*, suggests that CFE 34 (SEQ ID NO:143), CFE 35 (SEQ ID NO:144), and 90 (SEQ ID NO:199) are polypeptides which mediate a fatty acid biosynthesis pathway (Figure 19)

The comparison suggests that CFE 34 is a malonyl CoA:ACP transacylase, which catalyzes the reaction in which malonyl CoA and acyl carrier protein (ACP) are converted to malonyl-ACP and CoA. Thus, the CFE 34 polypeptide may be a homologue of *E. coli* FabD.

The comparison suggests that CFE 90 is a 3-oxoacyl-ACP synthase II (beta ketoacyl-ACP synthase II) which catalyzes the reaction in which malonyl-ACP is converted to beta aceto acetyl-ACP. Thus, the CFE 90 polypeptide may be a homologue of *E. coli* FabF.

The comparison suggests that CFE 35 is a 3-oxoacyl-ACP reductase (beta aceto acetyl ACP reductase) which catalyzes the reaction in which beta-keto-acetyl-ACP is converted to beta-hydroxy-acetyl-ACP. Thus, the CFE 35 polypeptide may be a homologue of *E. coli* FabG.

### Size Exclusion Chromatography

The estimated molecular weights of 2CFE 34 (SEQ ID NO:361), 2CFE 35 (SEQ ID NO:362), and 2CFE 90 (SEQ ID NO:413) were determined using the Biosil SEC-125 HPLC Gel Filtration column as described in Example 8, *supra*.

The results suggest that 2CFE 34 polypeptide is a monomeric protein (33,093 Da), 2CFE 35 is a trimeric protein (25,758 Da; approximately 85%), and 2CFE 90 is a dimeric protein (43,930 Da). Selected eluted samples of 2CFE 34 were electrophoresed on a polyacrylamide gel (Figure 20).

Biochemical Assay: CFE 34

The function of 2CFE 34 was determined by performing various biochemical reactions.  
5 To determine whether 2CFE 34 catalyzes the conversion of malonyl-CoA to malonyl and CoA, the following reaction was performed.

The biochemical reaction was performed in the presence of acyl carrier protein. The reaction included the following: 10  $\mu\text{M}$   $^{14}\text{C}$  labeled malonyl-CoA, 20  $\mu\text{M}$  ACP, 30  $\mu\text{M}$  10 2CFE 34 (e.g., FabD) in 20 mM Tris-Cl, pH 8.0 and 5 mM DTT in 300  $\mu\text{l}$  volume. The reaction was performed at room temperature (e.g., approximately 24 degrees C) for 30 minutes. The reaction was terminated with the addition of 45  $\mu\text{l}$  of 0.5% TFA. The labeled reaction was injected onto a MonoQ 5/5 column on a Gilson HPLC. Detection was performed by monitoring the radioactivity of the continuous flow-through of the 15 HPLC effluent. Chromatography was performed using a buffer gradient for column elution. Buffer A included 20 mM Tris-Cl, pH 8.3. Buffer B was the same as Buffer A and included 1 M NaCl. The program was held at 90% A, 10% B for 10 minutes followed by a linear ramp to a final mix of 50% of each Buffer A and B over 10 minutes.

20 The substrate (e.g.,  $^{14}\text{C}$  malonyl-CoA) eluted at 9.9 minutes, the product (e.g.,  $^{14}\text{C}$  malonyl-ACP) eluted at 14.3 minutes. The results indicate that CFE 34 catalyzes the conversion of malonyl-CoA and acyl carrier protein (ACP) to malonyl-ACP and CoA.

**EXAMPLE 15**

25

The following provides a description of the methods used to characterize CFE polypeptides 40, 41, and 46.

Computer-Aided Comparison

The computer-aided comparison, as described in Example 9 *supra*, suggests that the CFE 40 polypeptide (SEQ ID NO:149) is a phosphomethylpyrimidine (HMP-P) kinase  
5 involved in thiamine biosynthesis.

The comparison, as described in Example 9 *supra*, suggests that the CFE 41 polypeptide (SEQ ID NO:150) has a GTP-binding motif and may be a protease.

10 The comparison, as described in Example 9 *supra*, suggests that the CFE 46 polypeptide (SEQ ID NO:155) has an ATP-binding motif.

Affinity Purification of CFE 41

15 The large-scale method described in Example 5 *supra* (e.g., IPTG-induced protein production) was used to prepare a sample of 2CFE 41 polypeptide (SEQ ID NO:368). The sample was affinity purified using the Ni-NTA method described in Example 6, *supra*. The eluted fractions were loaded onto and run on a 12% SDS-PAGE gel (Novex) (Figure 21).

20

Circular Dichroism and Circular Dichroism Thermal Melt Analysis

Circular dichroism and circular dichroism thermal melt methods were performed using JASCO instrumentation. The concentration of the isolated 2CFE 40 (SEQ ID NO:367)  
25 was approximately 21  $\mu$ M, in a 0.1 cm pathlength cell at 210 nm. The circular dichroism spectrum suggests that this preparation of 2CFE 40 had mixed alpha and beta secondary structure. The circular dichroism thermal melt spectrum suggests that 2CFE 40 has a  $T_m$  of approximately 67 degrees C. The 2CFE 40 polypeptide precipitates at approximately the  $T_m$ .

The concentration of the isolated 2CFE 41 (SEQ ID NO:368) was approximately 70  $\mu$ M, in a 0.02 cm pathlength cell. The circular dichroism spectrum suggests that this preparation of 2CFE 41 had mixed alpha and beta secondary structure, with a greater  
5 percentage of alpha structures. The circular dichroism thermal melt spectrum suggests that 2CFE 41 has a  $T_m$  of approximately 38 degrees C. The 2CFE 41 polypeptide precipitates at approximately the  $T_m$ .

The concentration of the isolated 2CFE 46 (SEQ ID NO:373) was approximately 23  $\mu$ M,  
10 in a 0.1 cm pathlength cell at 280 nm. The circular dichroism spectrum suggests that this preparation of 2CFE 46 had mixed alpha and beta secondary structure. The circular dichroism thermal melt spectrum suggests that 2CFE 46 is highly stable at elevated temperatures. At 90 degrees C, the 2CFE 46 polypeptide exhibited only a 27% loss in signal and the polypeptide remained soluble.

15

#### Capillary Electrophoresis

Capillary electrophoresis was performed on samples of purified 2CFE 40, 41 and 46. The electropherograms of 2CFE 40, 41, and 46 are shown in Figure 22.

20

#### **EXAMPLE 16**

The following provides a description of methods that can be used to characterize CEG polypeptides (e.g., CFE polypeptides).

25

#### Computer-Aided Compilation

Computer-aided compilation of bacterial metabolic pathways may be analyzed using Pathway Tools from Doubletwise, based on the EcoCyc system (Karp P.D., et al., 1999  
30 *Nucleic Acids Res.* 1999 27(1):55-58). This analysis may be used to predict which CFEs mediate various steps of the pathways. This information may be used in combination

with the results of a binding reaction which identifies a ligand or substrate that binds with a CFE polypeptide.

#### Identifying the Function of a CFE Polypeptide

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The function of a CFE polypeptide may be identified by identifying a ligand or substrate which binds with the CFE polypeptide. The ligand or substrate may be identified using fractionation and affinity capillary electrophoresis methods. The following method is based upon the assumption that the bacterial cell lysate includes the ligand or substrate.

10

A bacterial host cells carrying an endogenous (e.g. native) CFE gene or carrying a recombinant vector which includes a CFE gene may be cultured so that the CFE polypeptide is produced by the cell. The cells may be ruptured in order to obtain the cell lysate. The cell lysate may be fractionated using HPLC technology. The HPLC fractions may be reacted with a CFE polypeptide in a binding reaction, and the binding reaction may be analyzed by affinity capillary electrophoresis methods. The ligand or substrate which reacts with the CFE polypeptide may be identified using mass spectrophotometry methods (in "Mass Spectrometry" 1990 eds. McCloskey, J. A., in *Methods in Enzymology* volume 193; Henion, J., et al., 1993 "Mass Spectrometric Investigations of Drug-Receptor Interactions" *Ther. Drug Monit.* 15:563-569; Loo, J. A., et al., 1999 "Application of Mass Spectrometry for Target Identification and Characterization" *Med. Res. Rev.* 19:307-319; Nguyen, D. N., et al., 1995 "Protein Mass Spectrometry: Applications to Analytical Biotechnology" *J. Chromatogr.* 705:21-45).

#### 25 **EXAMPLE 17**

The following provides a description of nuclear magnetic resonance (NMR) spectroscopy methods that were used to characterize CFE polypeptides.

30 High resolution NMR spectroscopy was applied to  $^{15}\text{N}$ -labeled,  $^{13}\text{C}/^{15}\text{N}$ -labeled,  $^2\text{H}/^{13}\text{C}/^{15}\text{N}$ -labeled, and type-specifically isotopically labeled CFE polypeptide samples

in the solution state for the following purposes: to assess various aspects of the structural state, e.g., foldedness, structural integrity; to refine a previously determined experimental structure of a close sequence homologue; to refine a homology-modeled structure; to assess the potential for a CFE polypeptide to bind small molecules; and to identify small-molecule pharmacophoric fragments that bind specifically to the CFE polypeptide ("Nuclear Magnetic Resonance" 1994 eds. James, T. L. in *Methods in Enzymology* volume 239).

The NMR analysis includes screening both a compound deck of approximately 4,500 commercially available, structurally and chemically diverse compounds (the small-molecule pharmacophore deck) and a compound deck of proprietary, known, anti-microbial compounds (anti-microbial deck) against the CFE polypeptides (i.e., target polypeptides) to determine, either based upon perturbations to the chemical shifts of the amide proton and/or nitrogen resonances, as measured from a two-dimensional proton-nitrogen heteronuclear single-quantum correlation spectrum (2D screening method), or based upon increases in the linewidth of the compound's proton resonance(s), as measured by a one-dimensional  $T_{1\rho}$  spin-lock difference spectrum (1D screening method), both whether a compound binds to a CFE polypeptide and, in the case of the 2D screening method, where the compound binds on the CFE polypeptide.

#### Isotopic Labeling of CFE Polypeptides

BL21-DE3 *E. coli* bacteria are transformed with the CFE expression vectors. Expression takes place between 20°C and 37°C in minimal media containing [ $^{15}\text{N}$ ]-ammonium sulfate as the sole nitrogen source and either glucose, [ $^2\text{H}$ ] $_{13}$ -glucose, or [ $^{13}\text{C}$ ] $_6$ -glucose as the sole carbon source. Glucose is used for preparing uniformly  $^{15}\text{N}$ -labeled and  $^2\text{H}/^{15}\text{N}$ -labeled CFE polypeptides. [ $^2\text{H}$ ] $_{13}$ -glucose is used for preparing type-specifically  $^1\text{H}/^{13}\text{C}$ -labeled, uniformly  $^{15}\text{N}$ -labeled CFE polypeptides. [ $^{13}\text{C}$ ] $_6$ -glucose is used for preparing  $^{13}\text{C}/^{15}\text{N}$ -labeled CFE polypeptides. The minimal media is prepared in 100%  $\text{H}_2\text{O}$  for expressing both uniformly  $^{15}\text{N}$ -labeled and uniformly  $^{13}\text{C}/^{15}\text{N}$ -labeled CFE polypeptides; the minimal media is prepared in 95%  $\text{D}_2\text{O}$  (deuterium oxide) and 5%  $\text{H}_2\text{O}$  for expressing



both type-specifically  $^1\text{H}/^{13}\text{C}$ -labeled, uniformly  $^{15}\text{N}$ -labeled and just uniformly  $^2\text{H}/^{15}\text{N}$ -labeled CFE polypeptides. In the case of type-specifically  $^1\text{H}/^{13}\text{C}$ -labeled, uniformly  $^{15}\text{N}$ -labeled CFE polypeptides, 40 mg/L of protonated and uniformly  $^{13}\text{C}/^{15}\text{N}$ -labeled isoleucine, valine and leucine amino acids are added to the minimal media.

5

#### NMR Screening

Compounds in the anti-microbial deck are pre-dissolved to a target concentration of 16 mM in deuterated DMSO (dimethylsulfoxide) with each deck well containing only one  
10 compound. Compounds in the small-molecule, pharmacophore deck are pre-dissolved in deuterated dmso to a target concentration of 50 mM in groups of 8, i.e., each deck well contains 8 unique compounds with each compound at a target concentration of 50 mM.

3.5  $\mu\text{l}$  of compound is placed at the bottom of a well in a 96-well, screening plate. This  
15 well will be referred to as the compound screening well. Each compound screening well contains solution from only one deck well. 166.5  $\mu\text{l}$  of buffer is added to each compound screening well. 170  $\mu\text{l}$  of a CFE polypeptide solution, initially at a concentration ranging from 200-300  $\mu\text{M}$ , is added to each compound screening well; the contents of that well are then thoroughly mixed. The control screening well contains only 3.5  $\mu\text{l}$  of deuterated  
20 dmso. The screening plate is then centrifuged in a bucket rotor for 15 minutes at 3,500 rpm to insure that all particulate matter is at the bottom of the well.

The 2D screening method requires a single control screening well in which the compound solution consists only of deuterated DMSO. The 1D screening method requires a control  
25 screening well for each compound screening well. In the case of the 1D screening method, the control screening well is prepared identically to the compound screening well except that the 170  $\mu\text{l}$  of a CFE polypeptide solution is replaced by 170  $\mu\text{l}$  of buffer.

The screening plate is covered with aluminum foil and placed onto a rack of a Gilson  
30 liquid handler. The Gilson liquid handler, under computer control by the NMR host/data-acquisition software, is responsible for removing each sample from the screening plate,

injecting the sample into a high-resolution,  $^1\text{H}/^{15}\text{N}$  double-resonance NMR flow-probe, removing the sample from the flow-probe, and dispensing it back into the screening plate well from which the sample was originally removed. NMR data are collected on the sample while the sample resides in the NMR flow-probe. The type of NMR data  
5 collected depends upon whether the 2D or 1D screening method is being used.

#### Determining Structural Characteristics of a CFE Polypeptide

In assessing various aspects of the structural state of a CFE polypeptide, NMR was used  
10 to provide the following information. The proton 1D spectra and proton-nitrogen 2D correlation NMR spectra were used to assess the overall foldedness of a CFE polypeptide without actually describing in detail that folded state. Unfolded and substantially misfolded proteins produced distinct signatures in these two types of NMR spectra.

15 The chemical shift of most protein nuclei in either the set  $\{\text{H}_\text{N}, \text{H}_\alpha, \text{H}_\beta, \text{C}', \text{C}_\alpha, \text{C}_\beta, \text{N}\}$  or the set  $\{\text{H}_\text{N}, \text{C}', \text{C}_\alpha, \text{C}_\beta, \text{N}\}$  for perdeuterated (e.g.,  $^2\text{H}$ -labeled) proteins were determined by procedures well known in the art that involve collecting up to 10 triple-resonance NMR data sets. The protein secondary structure was delineated as either helical, turn or extended (e.g.,  $\beta$ -sheet) by measuring  $\Delta(\delta_{\text{C}_\alpha} - \delta_{\text{C}_\beta})$ ,  $\Delta\delta_{\text{C}'}$ , and  $\Delta\delta_{\text{H}_\alpha}$  where  $\delta$  refers to the  
20 chemical-shift value and  $\Delta$  refers to the difference between chemical-shift values measured in this protein and those measured for the same residue type in a random-coil (unstructured), tetrameric peptide.

This secondary-structure profile was generated in approximately 2-3 weeks per protein.

25 The secondary-structure profile was used to confirm the functional identity of a protein. It was also used to refine the list of possible functional identities of folds, predicted by various computational techniques including fold recognition which is associated with a protein or polypeptide.

NMR was used to generate folds of proteins or polypeptides for which both no structure was known of a sequence homologue and no structural homologue was discernible in the PDB by fold recognition techniques.

5    Refining a Structural Model

Nuclear Overhauser (NOE) data were used to refine both homology-modeled structured and previously determined experimental structures of close sequence homologues. This process took approximately 2-3 weeks per structure.

10

The CFE 88 polypeptide was characterized by NMR analysis to establish its secondary structure. The NMR data was used to filter the computer-aided threading analysis. The NMR-determined secondary structure for CFE 88 suggested that CFE 88 is structurally similar to 4-aminoimidazole carboxylase.

15

The characteristics of other CFE polypeptides were analyzed by NMR methods. A computer-aided threading analysis revealed that the N-terminal domain of the protein EGA, which both binds and hydrolyzes GTP, was both structurally similar and sufficiently similar in sequence to CFE 52 to suggest that CFE 52 had a similar function.

20

The NMR data of CFE 103 suggests that this polypeptide is unfolded. Circular dichroism spectra, as a function of temperature, also indicated that CFE103 was unfolded.

25    The CFES 2, 42, 43, 68 and 88 polypeptides were tested for their ability to bind potential inhibitor molecules by screening both the anti-microbial deck and the small-molecule, pharmacophore deck. CFE 34 was tested for its ability to bind potential inhibitor molecules by screening the anti-microbial deck.

Characterizing Small-Molecule Binding

NMR-based screening was used to measure binding against both the small-molecule, pharmacophore deck and the anti-microbial deck. Binding data from these screens  
5 allowed assessment of the propensity of a protein to bind small molecules. The binding data was also used to identify sites on the protein which are capable of binding small molecules. The binding data was also used to identify common pharmacophores among the compounds which bind.

10 Reverse screening refers to a process whereby known anti-microbial compounds, the microbial target of which is unknown, are screened by a general method, e.g., binding as assessed by NMR, to find a physical interaction with polypeptide targets previously determined to be essential to the bacteria (i.e., the CFEs). The reverse screening method was used to determine which CFE polypeptides bind to which compounds in the anti-  
15 microbial deck. The reverse screening method included the following. The compounds in a proprietary compound deck were screened for Minimal Inhibitory Concentration (e.g., MIC). The compounds exhibiting antimicrobial activity were designated active compounds. The CFE polypeptides were screened to determine which polypeptide bind to which active compounds. The CFE polypeptides which bound to the active  
20 compound(s) were confirmed, where possible, i.e., in cases where an in-vitro assay was possible to construct, as being inhibited in their function as a polypeptide by the active compound(s) by examination of the inhibition profile of the compound(s) against the CFE polypeptides. For additional confirmation, the effect of the compound on the microorganism harboring the CFE polypeptide was monitored (e.g., whole cell assays).  
25 The structure of the active compound was used as a basis to generate chemically-related compounds by iterative synthesis. The chemically-related compounds were tested in a screening assay for binding with CFE polypeptides. The active compounds and the chemically-related compounds of interest were the compounds which exhibited an increase in binding affinity for a CFE polypeptide and/or exhibited drug-like properties.

30

The results of the reverse screening are as follows. 127 compounds from the proprietary compound deck exhibited anti-microbial activity. 94 of these active compounds were selected based upon both lack of cytotoxicity and lack of excessive hydrophobicity. These 94 compounds were soluble to 16 mM in deuterated DMSO; these compounds  
5 were also deemed to be sufficiently soluble in aqueous buffer for both the 2D and 1D NMR screening methods.

This subset of 94 compounds was used in an NMR-based screen to determine which compound binds to which CFE polypeptide. The CFE 42 polypeptide bound two  
10 different compounds with  $K_d$ 's in the range of 0.2 to 1 mM; the CFE 43 polypeptide bound one compound with  $K_d \sim 30$ -50  $\mu$ M; the CFE 34 polypeptide bound 13 compounds, one of which inhibited the polypeptide function with  $IC_{50} < 10 \mu$ M.

The enzyme assay used to confirm the NMR results which suggested CFE 34 interaction  
15 with the compounds included the following: 10  $\mu$ M  $^{14}$ C-labeled malonyl CoA; 20  $\mu$ M ACP, 30 pM CFE 34; 20 mM Tris-Cl, pH 8.0; 5 mM DTT; in the presence of absence of 50  $\mu$ M of a compound solubilized at 40 mM in 100% DMSO and dilute 100-fold into 10% DMSO and further diluted 8-fold for a final concentration of 50  $\mu$ M in 1.25% DMSO. The reaction was performed at room temperature, the reaction was stopped with  
20 the addition of TFA. Two hundred  $\mu$ l of the reaction was injected onto a Mono Q 5/5 column. The chromatography conditions included: A) 20 mM Tris-Cl, pH 8.3; B) 20 mM Tris-Cl, pH 8.3, 1 M NaCl. Hold 10% B for 5 minutes, linear gradient from 10% B to 50%B in 10 minutes, back to 10% B in 1 minute, hold for 14 minutes to re-equilibrate. The reaction substrate ( $^{14}$ C- malonyl CoA) eluted at 9.9 minutes, the reaction product  
25 ( $^{14}$ C-malonyl ACP) eluted at 14.3 minutes.

What is claimed is:

1. An isolated nucleic acid molecule encoding a polypeptide which is (1) essential for the viability of a bacterial cell and (2) has at least any one of the functions of a  
5       pantothenate kinase, a Holliday Junction branch migration protein, a single  
      stranded DNA binding protein, a phosphoglucosamine mutase, an  
      acetyltransferase, an uridylyltransferase, a malonyl CoenzymeA:ACP transacylase,  
      a 3-oxoacyl-ACP synthase II, a 3-oxoacyl-ACP reductase, a  
      phosphomethylpyrimidine (HMP-P) kinase, a GTP binding protein, a ATP  
10       binding protein, or a 4-aminoimidazole carboxylase.
2. The isolated nucleic acid molecule of claim 1, wherein the nucleic acid molecule  
      is shown in SEQ ID NO:97 or Figure 115 and wherein the polypeptide is a  
      pantothenate kinase.
- 15       3. The isolated nucleic acid molecule of claim 1, wherein the nucleic acid molecule  
      is shown in SEQ ID NO:35, Figure 60, SEQ ID NO:19, or Figure 44, and wherein  
      the polypeptide is a Holliday Junction branch migration protein.
- 20       4. The isolated nucleic acid molecule of claim 1, wherein the nucleic acid molecule  
      is shown in SEQ ID NO:8 or Figure 33 and wherein the polypeptide is a single  
      stranded DNA binding protein.
- 25       5. The isolated nucleic acid molecule of claim 1, wherein the nucleic acid molecule  
      is shown in SEQ ID NO:3 or Figure 28 and wherein the polypeptide is a  
      phosphoglucosamine mutase.
- 30       6. The isolated nucleic acid molecule of claim 1, wherein the nucleic acid molecule  
      is shown in SEQ ID NO:82 or Figure 103 and wherein the polypeptide is a  
      acetyltransferase.

7. The isolated nucleic acid molecule of claim 1, wherein the nucleic acid molecule is shown in SEQ ID NO:82 or Figure 103 and wherein the polypeptide is a uridylyltransferase.
- 5 8. The isolated nucleic acid molecule of claim 1, wherein the nucleic acid molecule is shown in SEQ ID NO:30 or Figure 55 and wherein the polypeptide is a malonyl CoenzymeA:ACP transacylase.
9. The isolated nucleic acid molecule of claim 1, wherein the nucleic acid molecule is shown in SEQ ID NO:86 or Figure 107 and wherein the polypeptide is a 3-oxoacyl-ACP synthase II.
- 10 10. The isolated nucleic acid molecule of claim 1, wherein the nucleic acid molecule is shown in SEQ ID NO:31 or Figure 56 and wherein the polypeptide is a 3-oxoacyl-ACP reductase.
- 15 11. The isolated nucleic acid molecule of claim 1, wherein the nucleic acid molecule is shown in SEQ ID NO:36 or Figure 61 and wherein the polypeptide is a phosphomethylpyrimidine (HMP-P) kinase.
- 20 12. The isolated nucleic acid molecule of claim 1, wherein the nucleic acid molecule is shown in SEQ ID NO:37, Figure 62, SEQ ID NO:48, or Figure 73, and wherein the polypeptide is a GTP binding protein.
- 25 13. The isolated nucleic acid molecule of claim 1, wherein the nucleic acid molecule is shown in SEQ ID NO:42 or Figure 67 and wherein the polypeptide is a ATP binding protein.

14. The isolated nucleic acid molecule of claim 1, wherein the nucleic acid molecule is shown in SEQ ID NO:84 or Figure 105 and wherein the polypeptide is a 4-aminoimidazole carboxylase.
- 5 15. The isolated nucleic acid molecule of claim 1, wherein the nucleic acid molecule is shown in SEQ ID NO:48 or Figure 73 and wherein the polypeptide is a GTP binding protein.
- 10 16. An isolated nucleic acid molecule encoding a polypeptide which is essential for the viability of a bacterial cell, the nucleic acid molecule comprising a sequence shown in any one of SEQ ID NOS:1-113.
- 15 17. An isolated nucleic acid molecule encoding a polypeptide which is essential for the viability of a bacterial cell, the nucleic acid molecule comprising a sequence shown in any one of Figures 26-130.
18. An isolated nucleic acid molecule encoding any one of a polypeptide designated CFE 1-117 having the amino acid sequence shown in SEQ ID NO:114-226.
- 20 19. An isolated nucleic acid molecule comprising a nucleotide sequence which is complementary to the nucleotide sequence of claim 1, 16, 17 or 18.
20. The isolated nucleic acid molecule of claim 1, 16, 17 or 18 which is DNA or RNA.
- 25 21. The isolated nucleic acid molecule of claim 20, which is labeled with a detectable marker.
- 30 22. The isolated nucleic acid molecule of claim 21, wherein the detectable marker is selected from the group consisting of a radioisotope, a fluorescent compound, a



bioluminescent compound, a chemiluminescent compound, a metal chelator and an enzyme.

23. A vector comprising the nucleotide sequence of claim 1, 16, 17, or 18.

5

24. A host-vector system comprising the vector of claim 23, in a suitable host cell.

25. The host-vector system of claim 24, wherein the suitable host cell is selected from a group consisting of a yeast cell, a plant cell, and an animal cell.

10

26. The host-vector system of claim 24, wherein the suitable host cell is selected from a group consisting of an *Escherichia* cell, a *Bacillus* cell, a *Pseudomonas* cell, a *Streptococcus* cell, and a *Streptomyces* cell.

15

27. An isolated polypeptide which is essential for the viability of a bacterial cell comprising the amino acid sequence as shown in any one of SEQ. ID NOS: 114-226.

20

28. An isolated polypeptide which is essential for the viability of a bacterial cell encoded by the isolated nucleic acid molecule of claim 1, 16, 17, or 18.

29. The isolated polypeptide of claim 27 or 28 which is a fusion polypeptide.

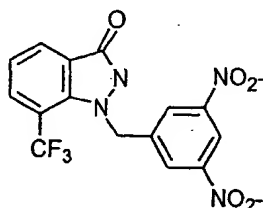
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30. A method for producing a polypeptide having the amino acid sequence of any one of SEQ ID NOS: 114-226 or a polypeptide encoded by the polynucleotide sequence as shown in any one of Figures 26-130, comprising:

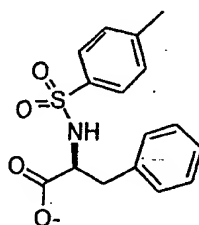
- a) culturing the host-vector system of claim 24 under suitable conditions so as to produce the polypeptide; and
- b) recovering the polypeptide so produced.

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31. A polypeptide produced by the method of claim 30.
32. A ligand which binds the polypeptide of claim 27 or 28.
- 5 33. The ligand of claim 32 which is an antibody or an immunologically active fragment thereof.
34. The ligand of claim 33, wherein the antibody is a monoclonal antibody.
- 10 35. The ligand of claim 32 which is a diazalactone.
36. The ligand of claim 35, wherein the diazalactone comprises the structure:

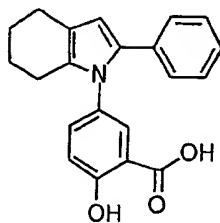


37. The ligand of claim 32 which is a *N*-protected amino acid.
- 15 38. The ligand of claim 37, wherein the *N*-protected amino acid comprises the structure:



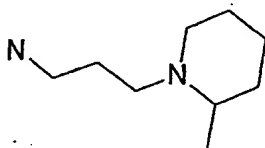
39. The ligand of claim 32 which is an azabicyclodiene.

40. The ligand of claim 39, wherein the azabicyclodiene comprises the structure:



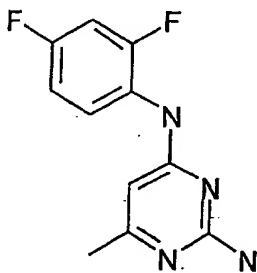
5 41. The ligand of claim 32 which is an alkaloid.

42. The ligand of claim 41, wherein the alkaloid comprises the structure:

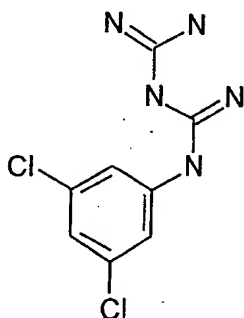


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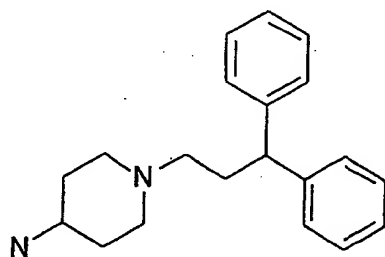
43. The ligand of claim 41, wherein the alkaloid comprises the structure:



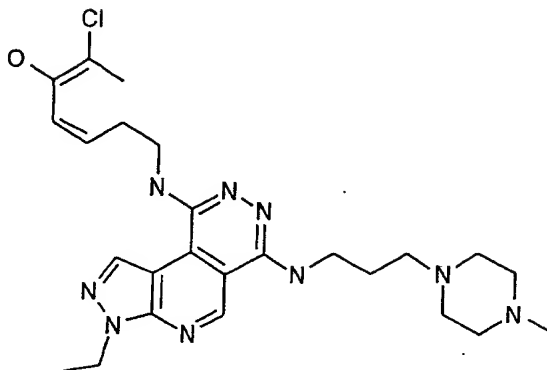
44. The ligand of claim 41, wherein the alkaloid comprises the structure:



5 45. The ligand of claim 41, wherein the alkaloid comprises the structure:

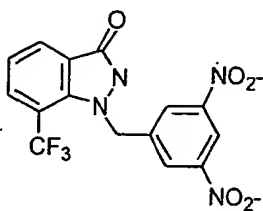


46. The ligand of claim 41, wherein the alkaloid comprises the structure:



- 5 47. A method for detecting the presence of the polypeptide of claim 27 or 28 in a sample, comprising contacting the sample with a ligand which binds the polypeptide and detecting the binding of the polypeptide with the ligand in the sample.
- 10 48. The method of claim 47, wherein the detecting comprises:
- a) contacting the sample with the ligand; and
  - b) determining whether a polypeptide-ligand complex is so formed.
- 15 49. The method of claim 47, wherein the sample is a cell, a tissue, or a biological fluid.
50. The method of claim 47, wherein the sample is blood, serum, a swab from nose, a swab from ear, or a swab from throat.
- 20 51. The method of claim 47, wherein the ligand is a diazalactone.

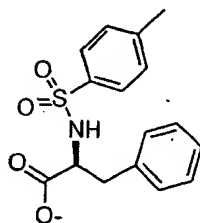
52. The method of claim 51, wherein the diazalactone comprises the structure:



53. The method of claim 47, wherein the ligand is a *N*-protected amino acid.

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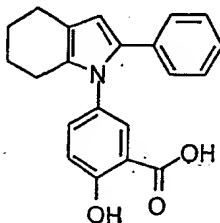
54. The method of claim 53, wherein the *N*-protected amino acid comprises the structure:



55. The method of claim 47, wherein the ligand is an azabicyclodiene.

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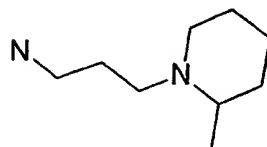
56. The method of claim 55, wherein the azabicyclodiene comprises the structure:



57. The ligand of claim 47 which is an alkaloid.

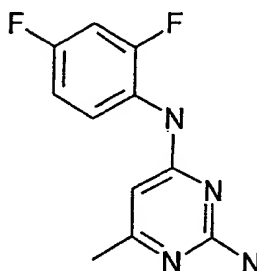
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58. The ligand of claim 57, wherein the alkaloid comprises the structure:



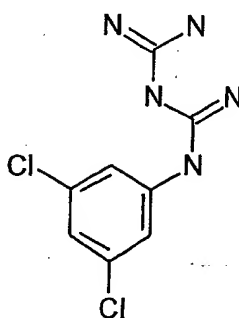
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59. The ligand of claim 57, wherein the alkaloid comprises the structure:

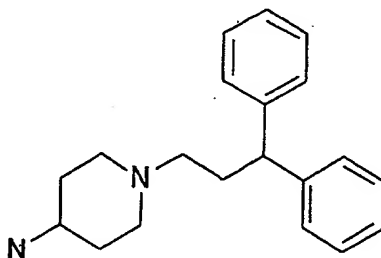


60. The ligand of claim 57, wherein the alkaloid comprises the structure:

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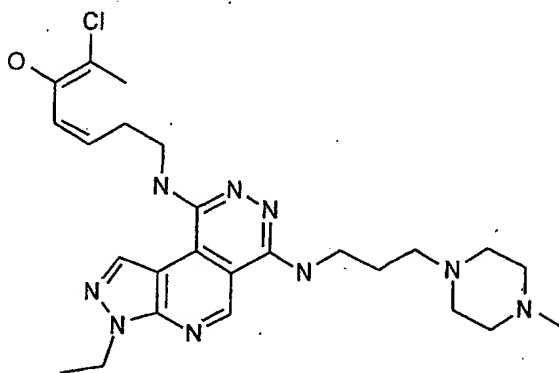


61. The ligand of claim 57, wherein the alkaloid comprises the structure:



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62. The ligand of claim 57, wherein the alkaloid comprises the structure:



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63. A method for detecting the presence of a target nucleic acid molecule as shown in any one of SEQ ID NOS:1-113 in a sample, comprising contacting the sample with the complementary nucleic acid molecule of claim 19 and detecting the binding of the target nucleic acid molecule with the complementary nucleic acid molecule in the sample.

15

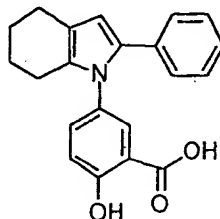


64. The method of claim 63, wherein the detecting comprises:
- a) contacting the sample with the complementary nucleic acid molecule; and
  - b) determining whether a complex comprising the target nucleic acid molecule and the complementary nucleic acid molecule is so formed.
65. The method of claim 63, wherein the sample is a cell, a tissue, or a biological fluid.
66. The method of claim 63, wherein the sample is blood, serum, a swab from nose, a swab from ear, or a swab from throat.
67. A pharmaceutical composition comprising the nucleic acid molecule of claim 1, 16, 17, or 18.
68. A pharmaceutical composition comprising the polypeptide of claim 27 or 28.
69. A pharmaceutical composition comprising the ligand of claim 32.
70. A method for determining whether a genomic nucleotide sequence of interest is essential for viability of a bacterial cell, comprising
- a. integrating an exogenous nucleotide sequence into the genomic nucleotide sequence of interest, wherein the exogenous nucleotide sequence comprises a portion of an open reading frame of the genomic nucleotide sequence of interest, and
  - b. determining whether the cell having the genomic nucleotide sequence of interest so integrated is viable.
71. The method of claim 70, wherein the portion of the open reading frame comprises about 200 to 500 base pairs in length.

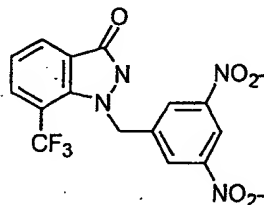
- 5 72. The method of claim 70, wherein the exogenous nucleotide sequence further comprises a nucleotide sequence conferring a selectable phenotype to the cell having the genome so integrated.
73. The method of claim 70, wherein determining comprises selecting the cell having the genome so integrated in the presence of a selection agent.
- 10 74. The method of claim 73, wherein the selection agent is chloramphenicol.
75. A nucleotide sequence of interest which is essential for viability of a bacterial cell isolated by the method of claim 70.
- 15 76. A bacterial cell comprising an exogenous nucleotide sequence integrated into the genomic nucleotide sequence of interest, generated by the method of claim 70.
- 20 77. A method for determining whether a genomic nucleotide sequence of interest resides within an operon, comprising
- a) integrating an exogenous nucleotide sequence into the genomic nucleotide sequence of interest; and
  - b) determining whether the cell having the genomic nucleotide sequence of interest so integrated is viable, and wherein the exogenous nucleotide sequence lacks an expression regulatory sequence.
- 25 78. The method of claim 77, wherein the exogenous nucleotide sequence further comprises a nucleotide sequence conferring a selectable phenotype to the cell having the genome so integrated.
- 30 79. The method of claim 77, wherein determining comprises selecting the cell having the genome so integrated in the presence of a selection agent.

80. The method of claim 79, wherein the selection agent is chloramphenicol.
- 5 81. A method for inhibiting a function of a CEG polypeptide which is essential for viability of a bacterial cell, the method comprising contacting the CEG polypeptide with the ligand of claim 32 under suitable conditions thereby inhibiting the function of the CEG polypeptide.
- 10 82. The method of claim 81, wherein the function of the CEG polypeptide is selected from a group consisting of a pantothenate kinase, a Holliday Junction branch migration protein, a single stranded DNA binding protein, a phosphoglucosamine mutase, an acetyltransferase, an uridylyltransferase, a malonyl CoenzymeA:ACP transacylase, a 3-oxoacyl-ACP synthase II, a 3-oxoacyl-ACP reductase, a phosphomethylpyrimidine (HMP-P) kinase, a GTP binding protein, a ATP
- 15 binding protein, or a 4-aminoimidazole carboxylase.
83. The method of claim 81, wherein the CEG polypeptide is selected from a group consisting of CFE1-113.
- 20 84. The method of claim 81, wherein the CEG polypeptide is 2CFE 34 shown in Figure 55.
85. The method of claim 81, wherein the CEG polypeptide is 2CFE 43 shown in
- 25 Figure 64.

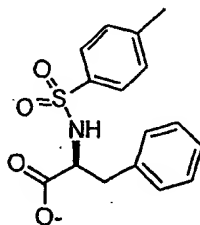
86. The method of claim 81, wherein the CEG polypeptide is 2CFE 34 shown in Figure 55 and the ligand is:



5 87. The method of claim 81, wherein the CEG polypeptide is 2CFE 43 shown in Figure 64 and the ligand is:



10 88. The method of claim 81, wherein the CEG polypeptide is 2CFE 43 shown in Figure 64 and the ligand is:



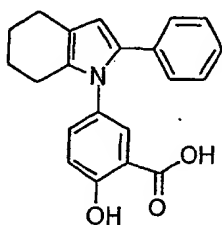
89. A method for identifying a ligand in a sample which specifically binds a CEG polypeptide, the method comprising:

- a) contacting the CEG polypeptide with the sample under suitable conditions so that a complex having the CEG polypeptide and the ligand is formed;
- b) recovering the complex so formed ; and
- c) separating the CEG polypeptide from the ligand in the complex and identifying the ligand so separated.

90. The method of claim 89, wherein the sample is a tissue or biological fluid.

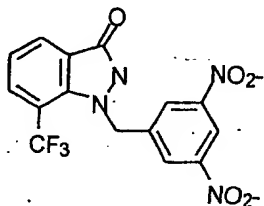
91. The method of claim 89, wherein the ligand is an azabicyclodiene.

92. The method of claim 91, wherein the azabicyclodiene comprises the structure:



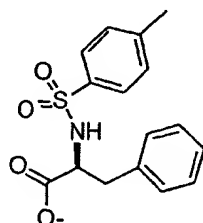
93. The method of claim 89, wherein the ligand is a diazalactone.

94. The method of claim 93, wherein the diazalactone comprises the structure:



95. The method of claim 89, wherein the ligand is a *N*-protected amino acid.

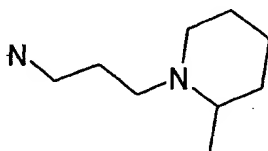
96. The method of claim 95, wherein the *N*-protected amino acid comprises the structure:



5

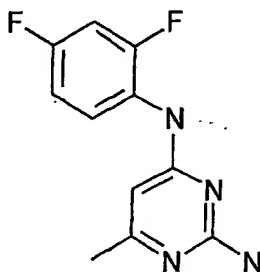
97. The method of claim 89, wherein the ligand is an alkaloid.

98. The ligand of claim 97, wherein the alkaloid comprises the structure:



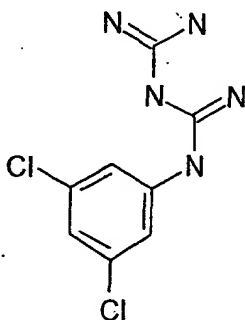
10

99. The ligand of claim 97, wherein the alkaloid comprises the structure:



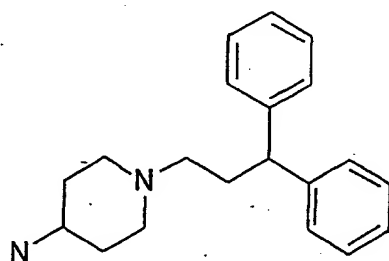
15

100. The ligand of claim 97, wherein the alkaloid comprises the structure:

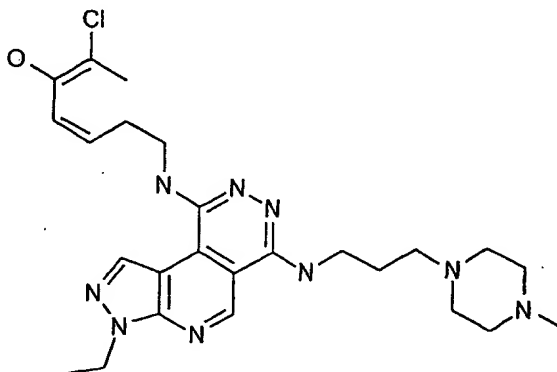


101. The ligand of claim 97, wherein the alkaloid comprises the structure:

5

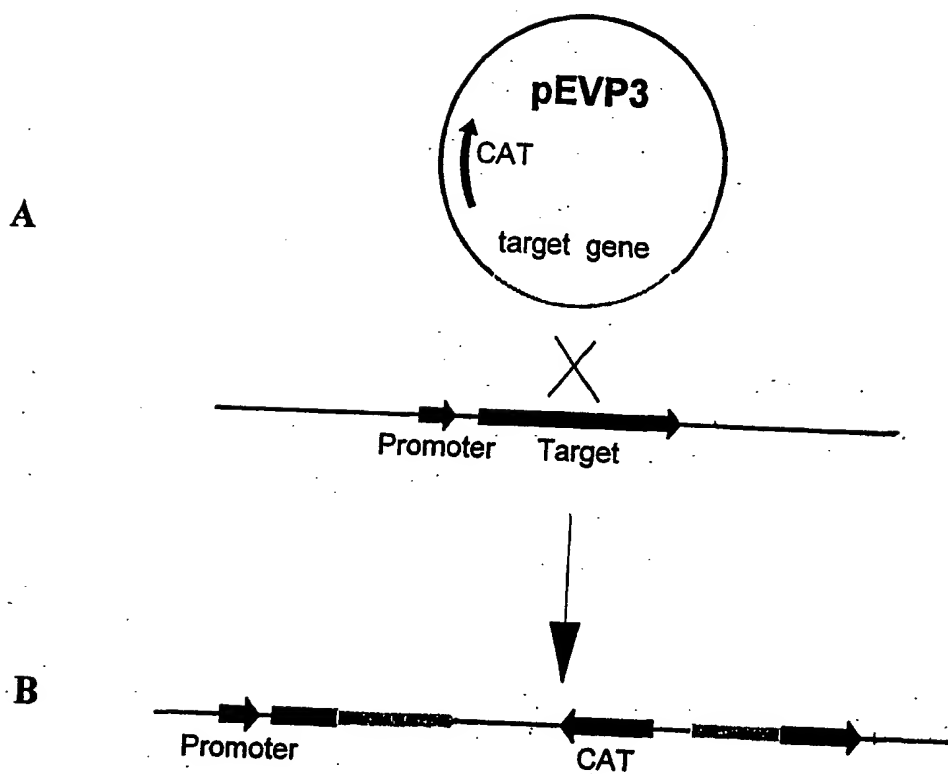


102. The ligand of claim 97, wherein the alkaloid comprises the structure:



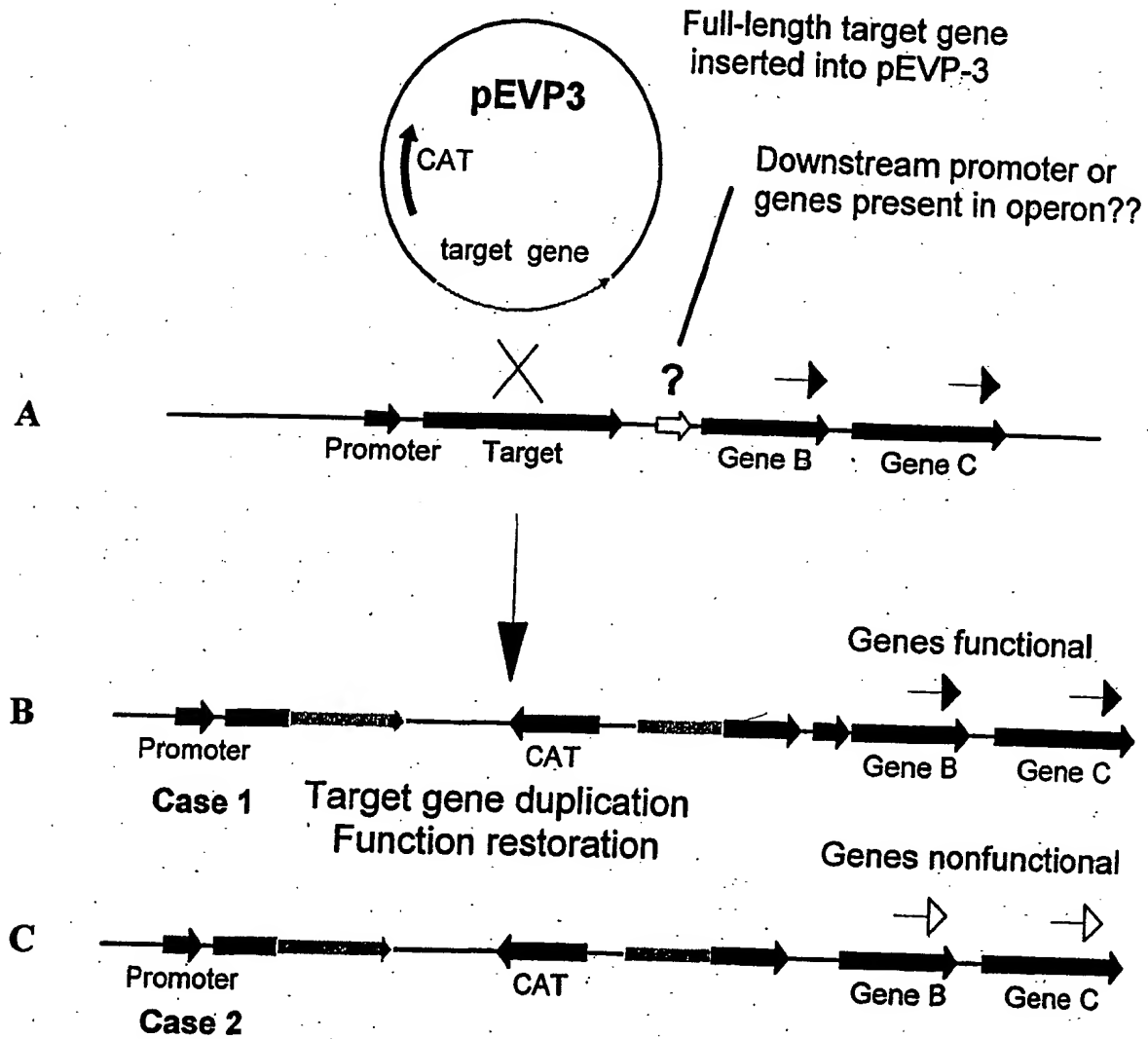


# Gene Disruption Assay



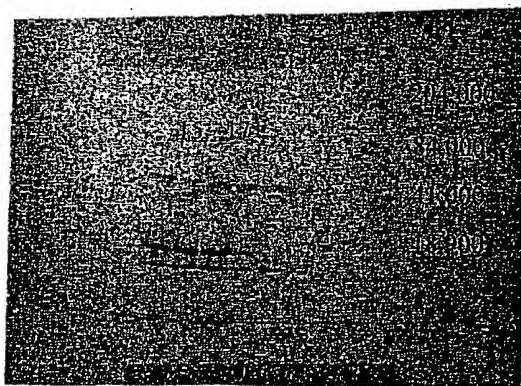
**FIGURE 1**

# Polarity test for Operons



**FIGURE 2**

A.

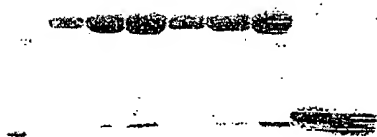


B.

204,000

12 24 36

41,000



17,000-MW proteins

FIGURE 3

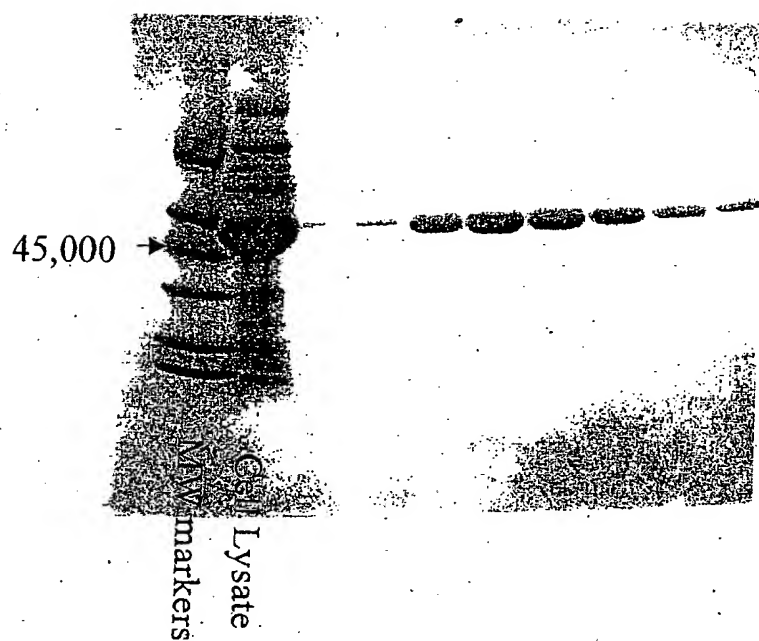


FIGURE 4

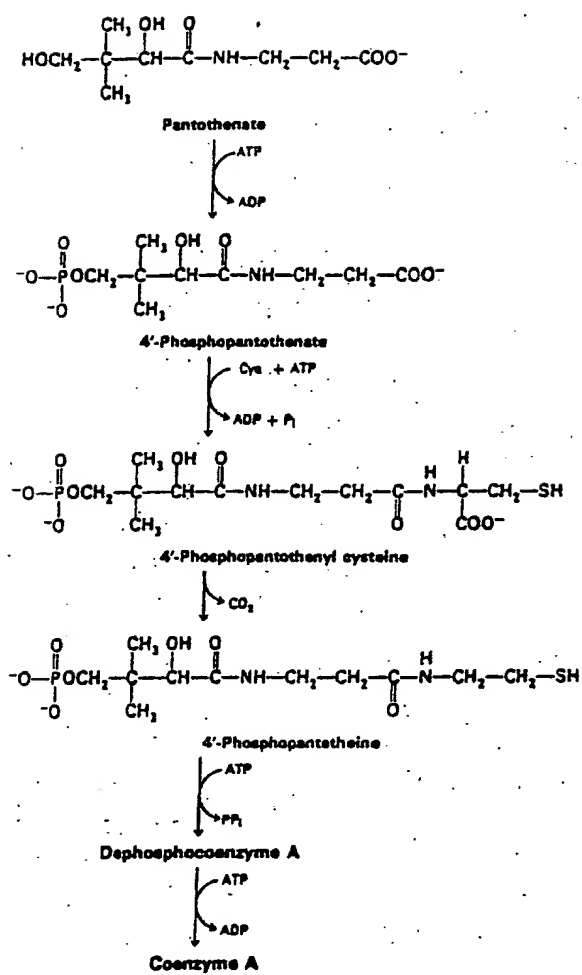
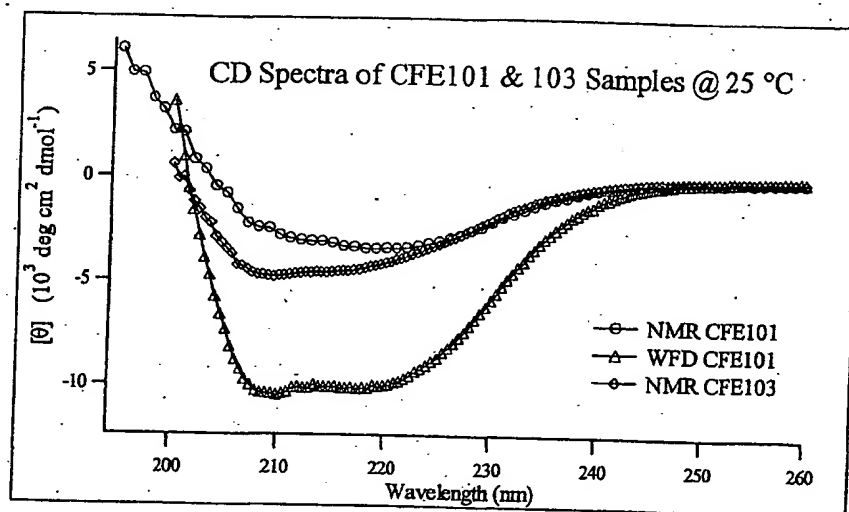


FIGURE 5

A.



B.

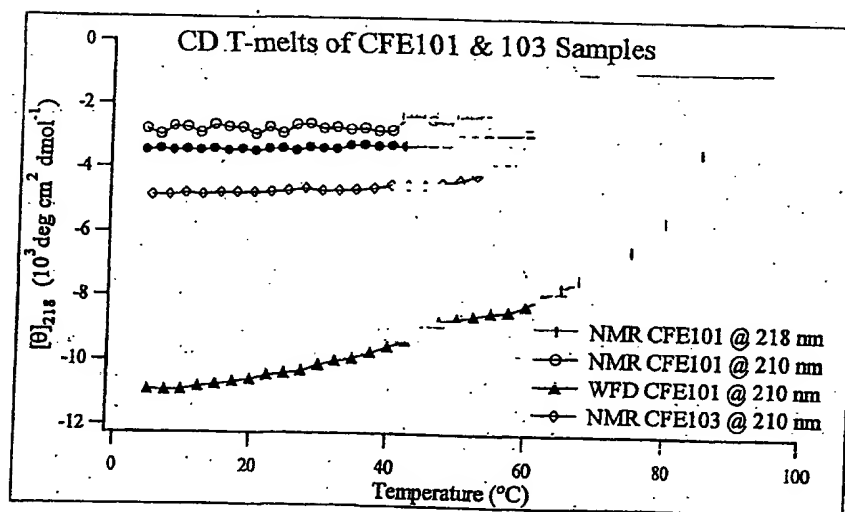
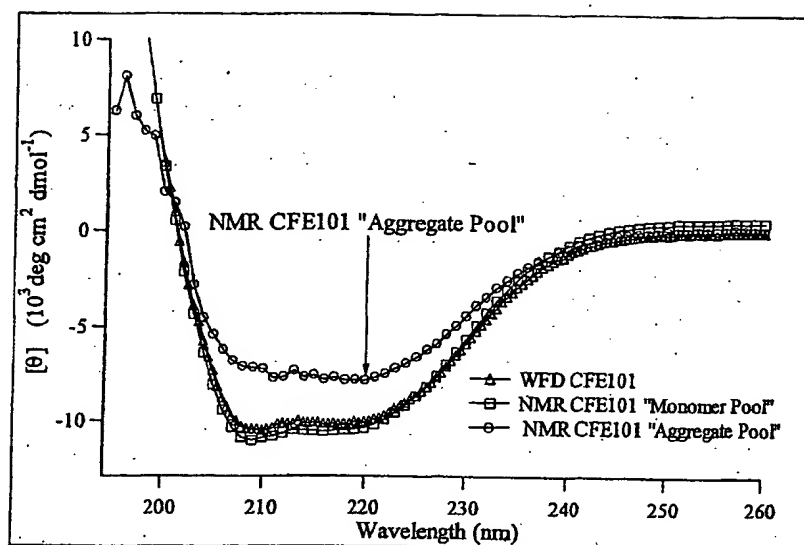


FIGURE 6

A.



B.

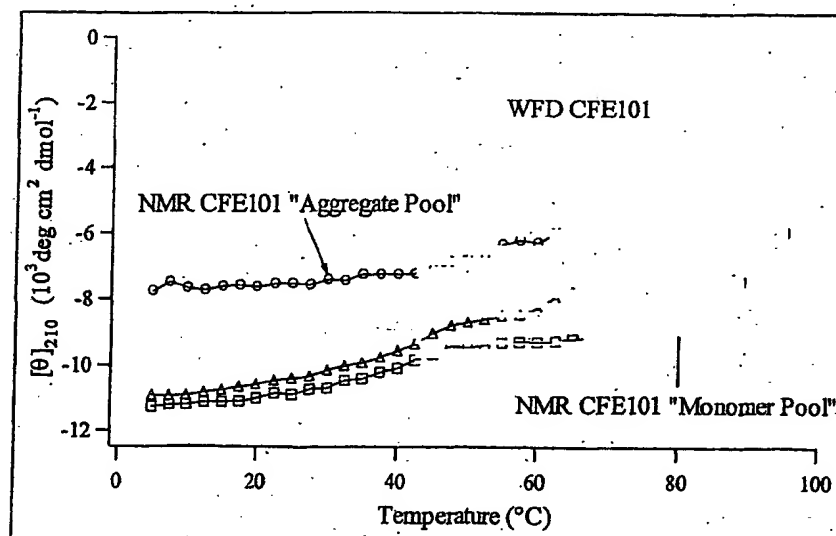


FIGURE 7

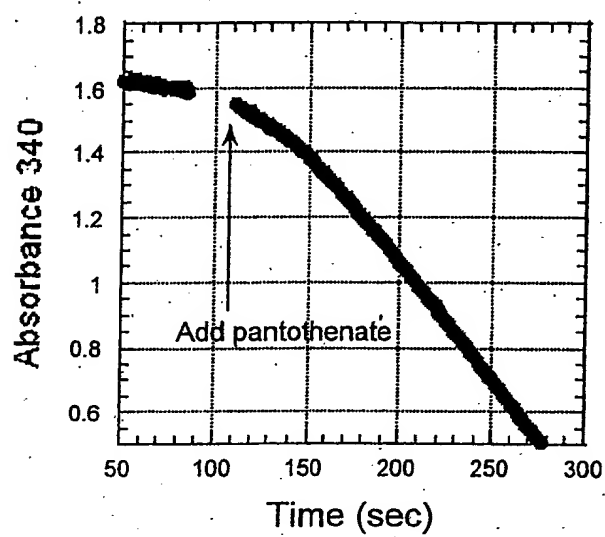


FIGURE 8



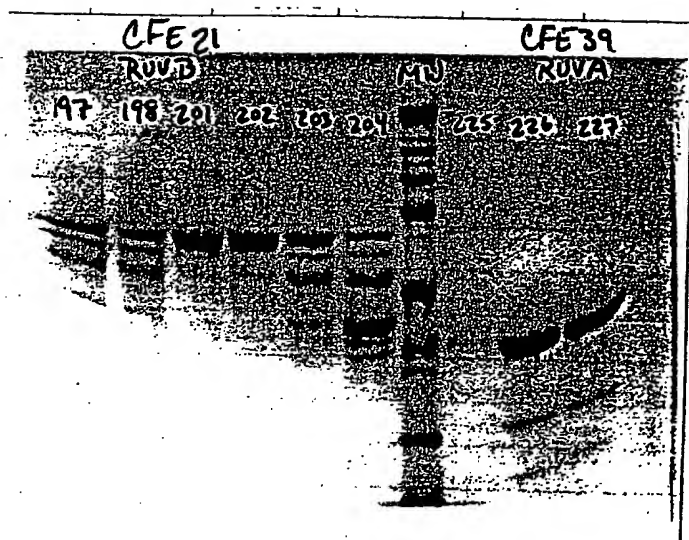


FIGURE 9

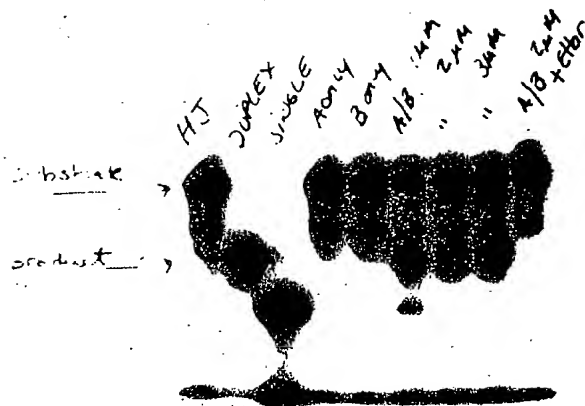


FIGURE 10

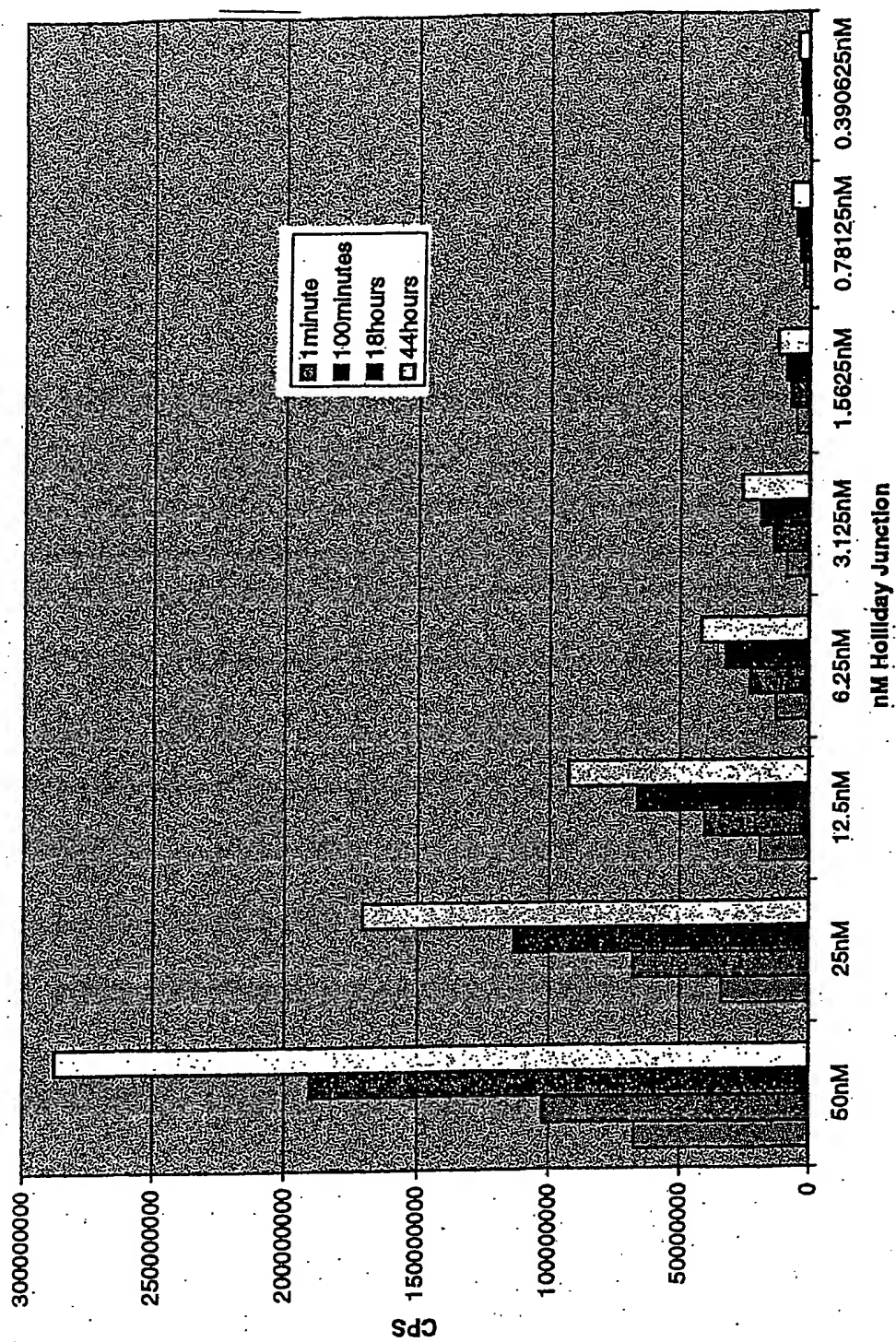


FIGURE 11

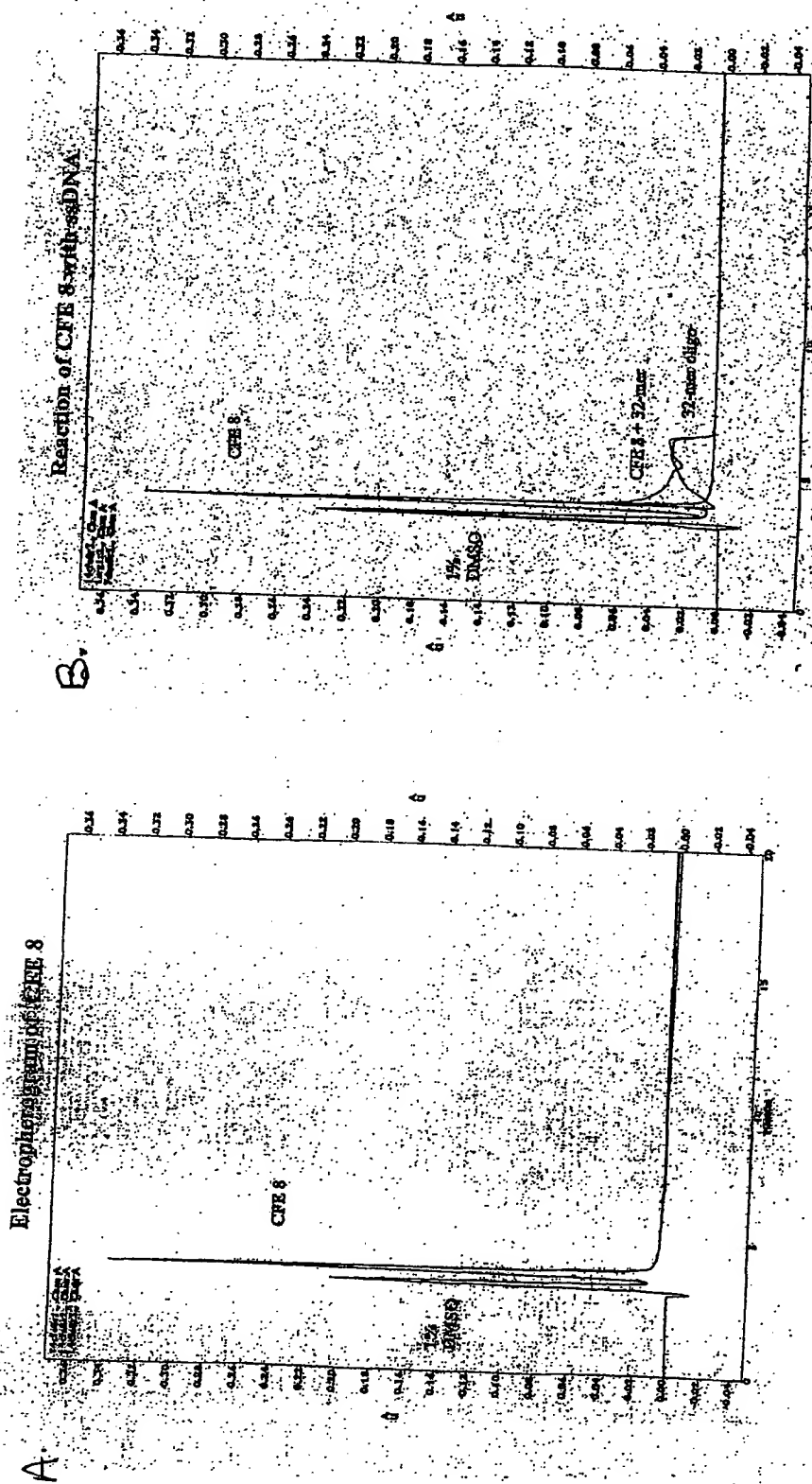


FIGURE 12

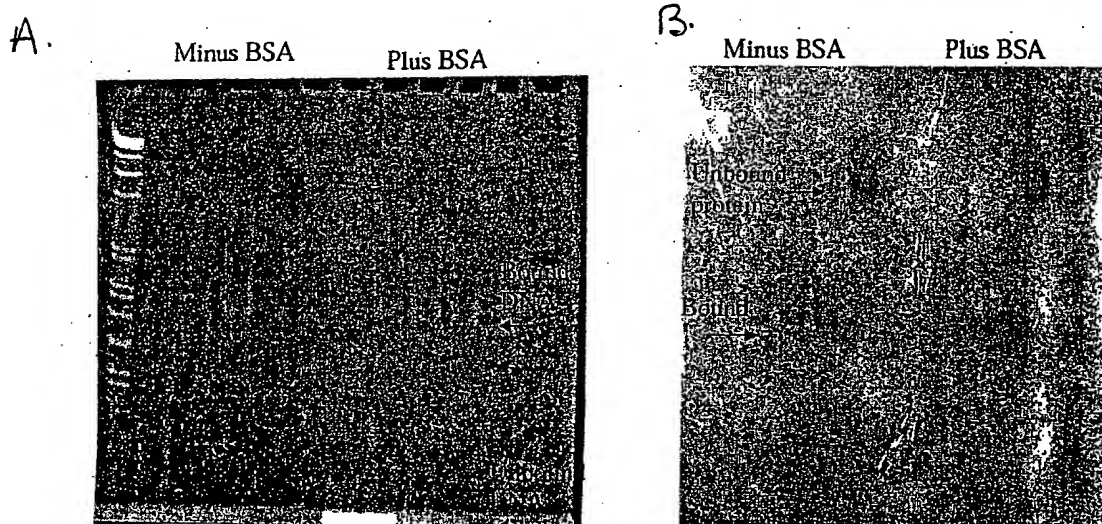


FIGURE 13

## N-Acetyl Glucosamine Pathway

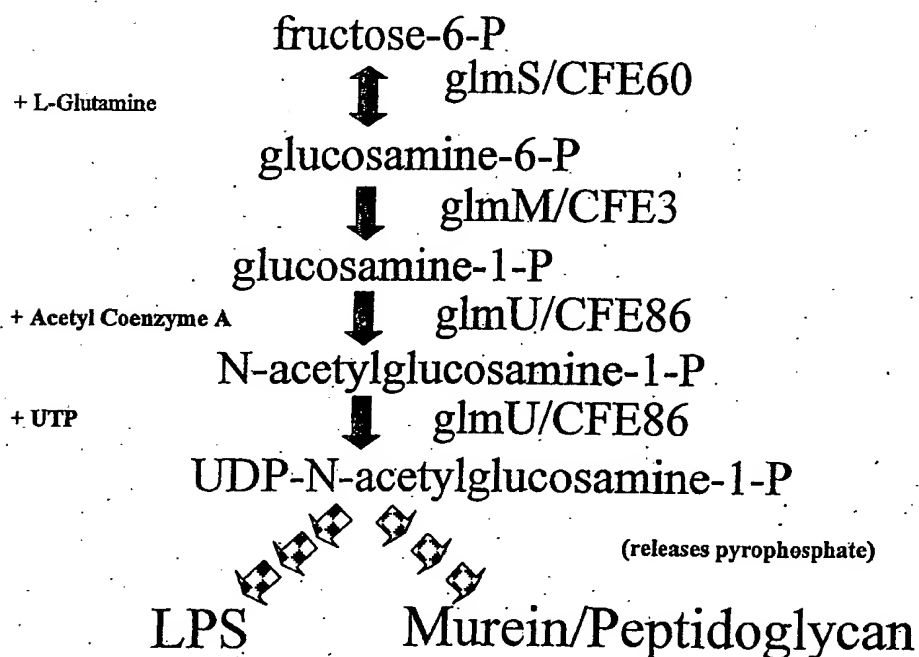


FIGURE 14

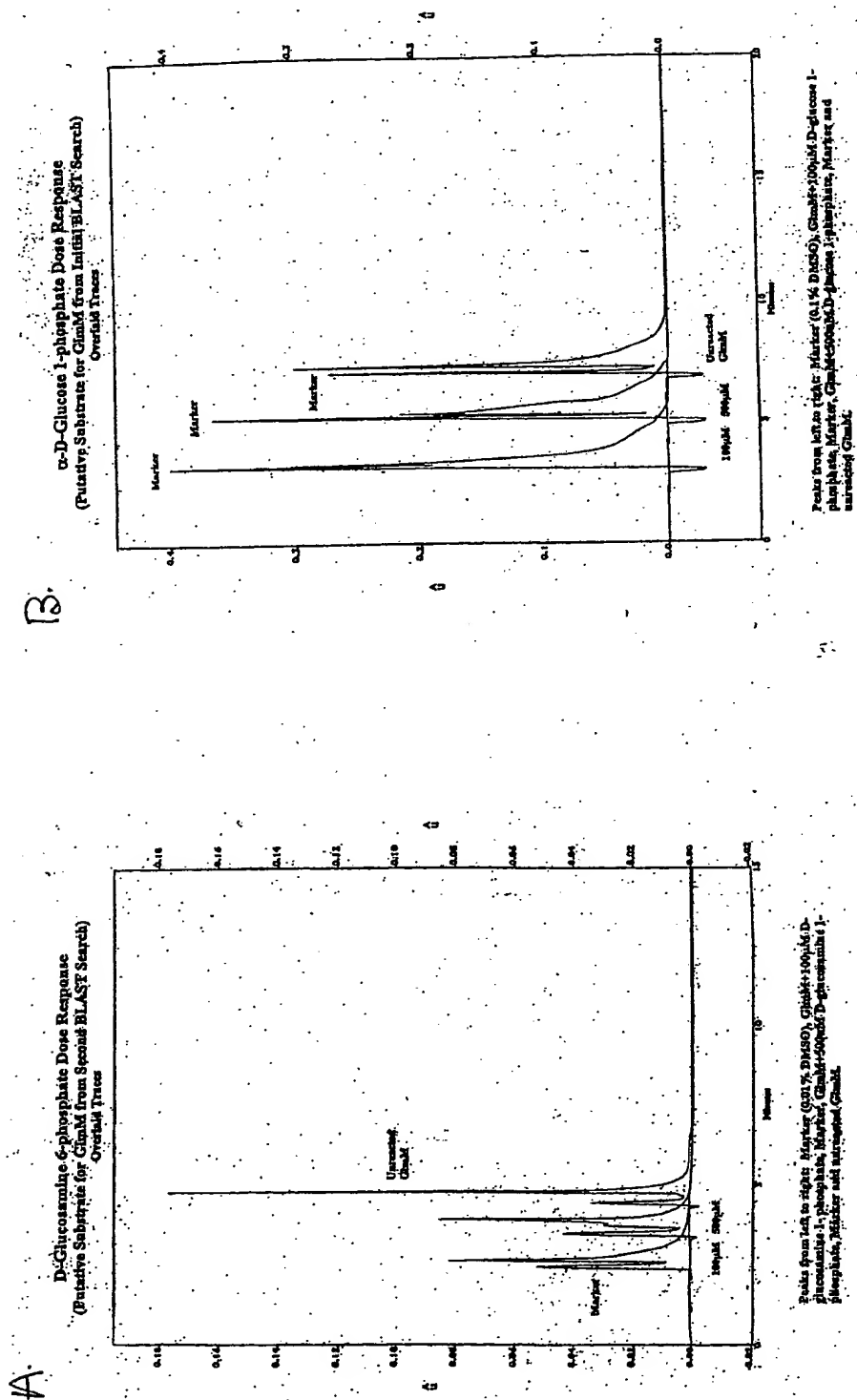


FIGURE 15

C:

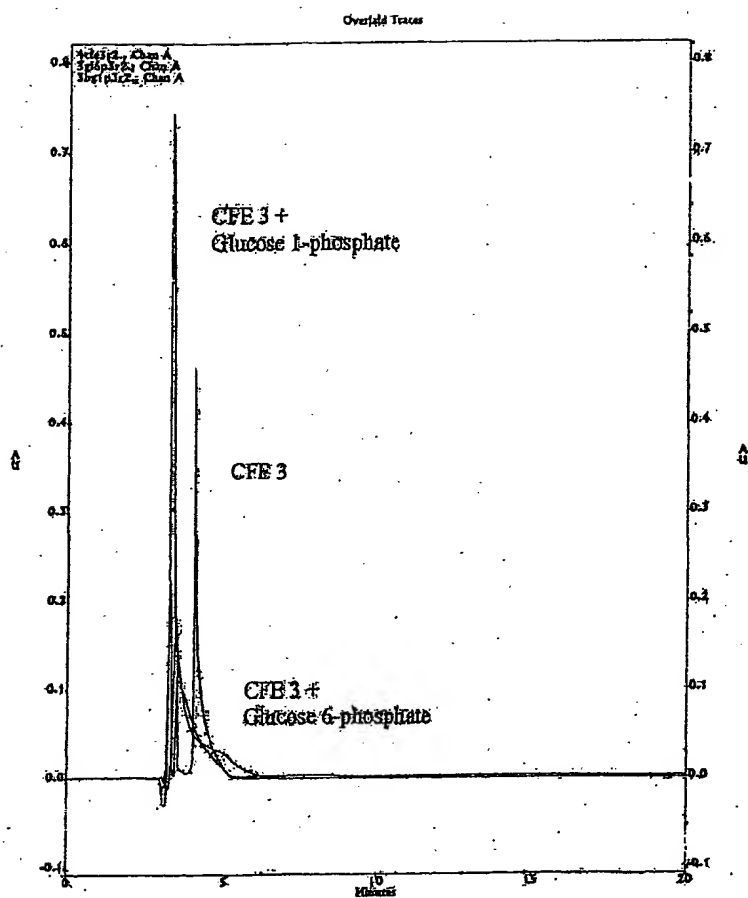


FIGURE 15



D.

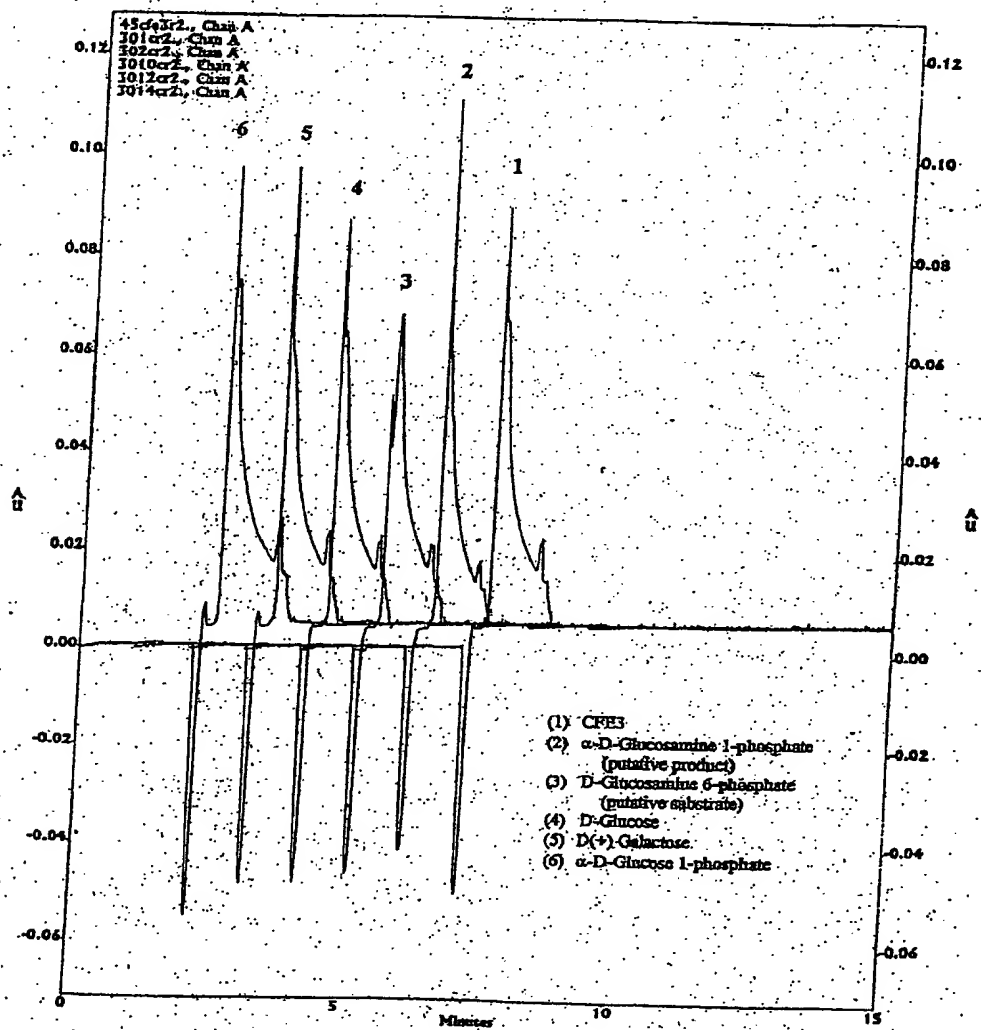


FIGURE 15

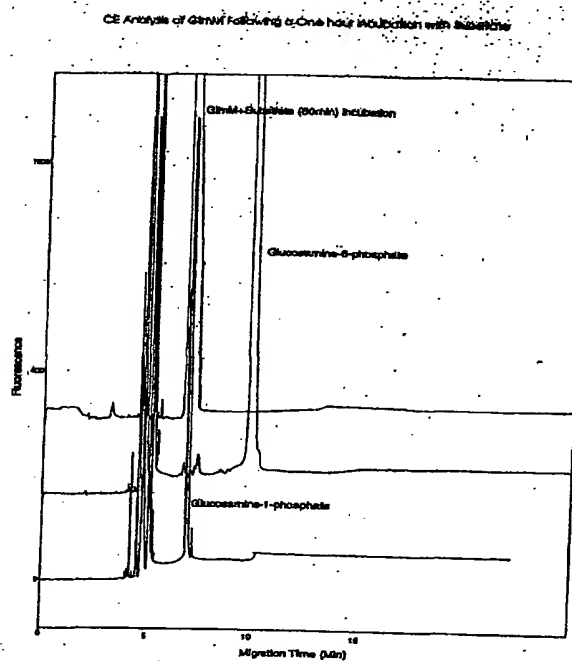


FIGURE 16

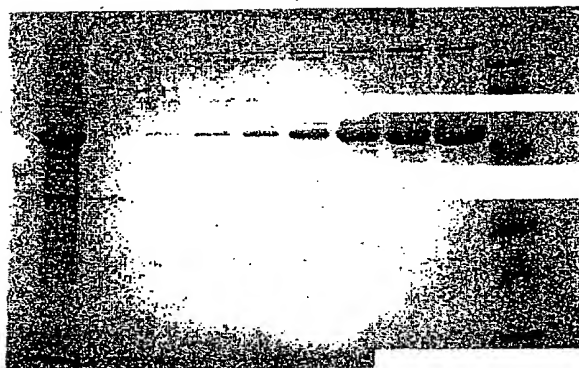


FIGURE 17

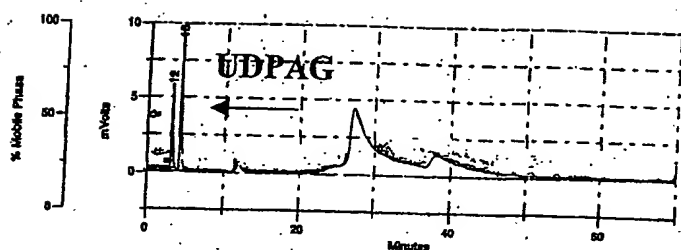


FIGURE 18

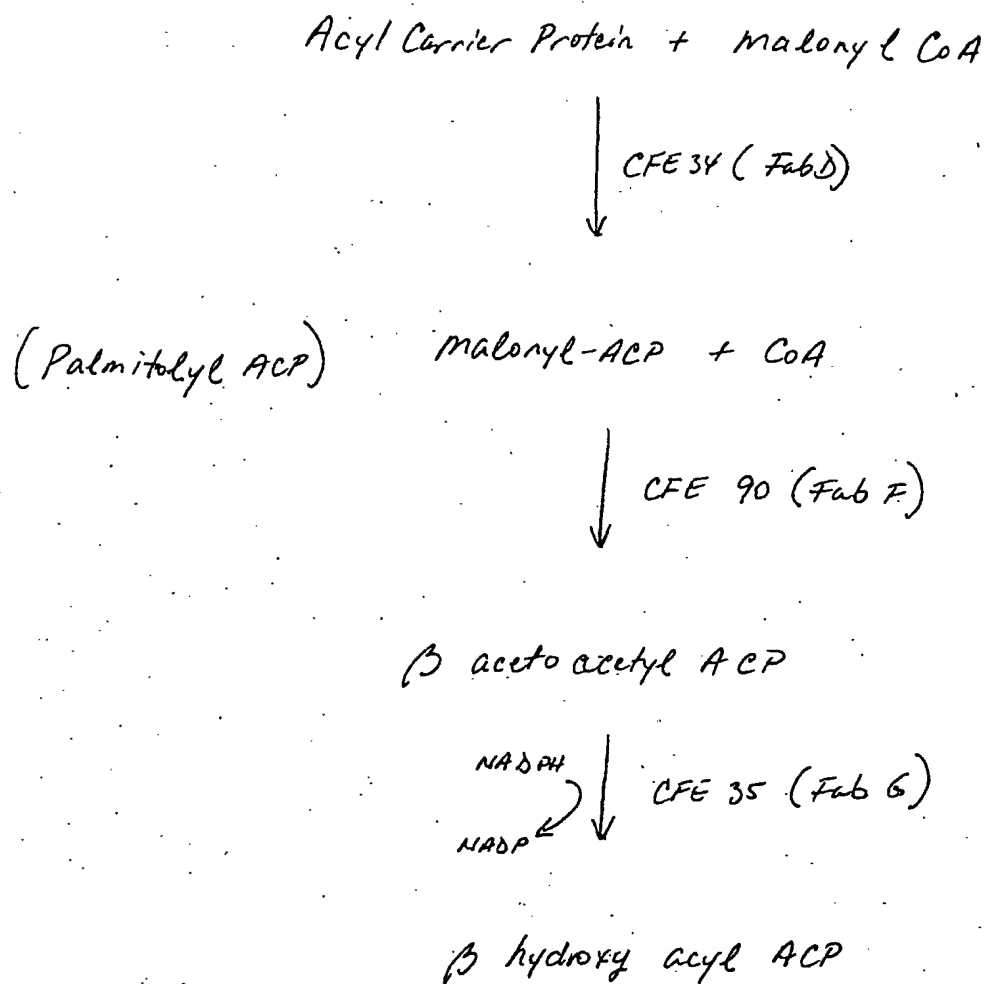


FIGURE 19.

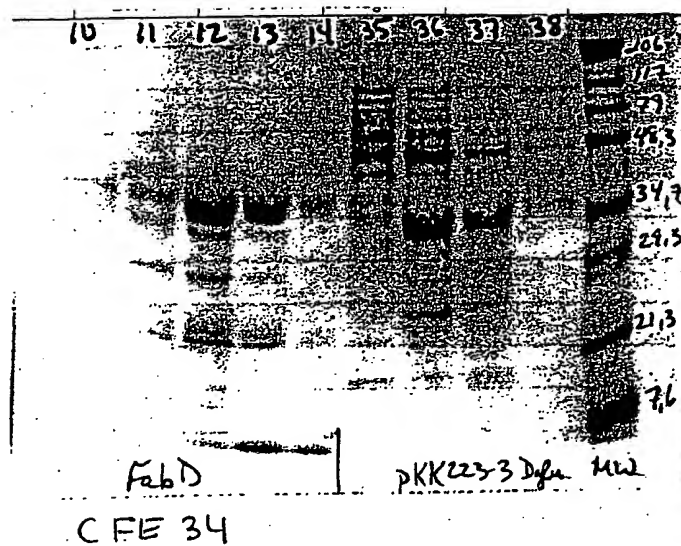


FIGURE 20

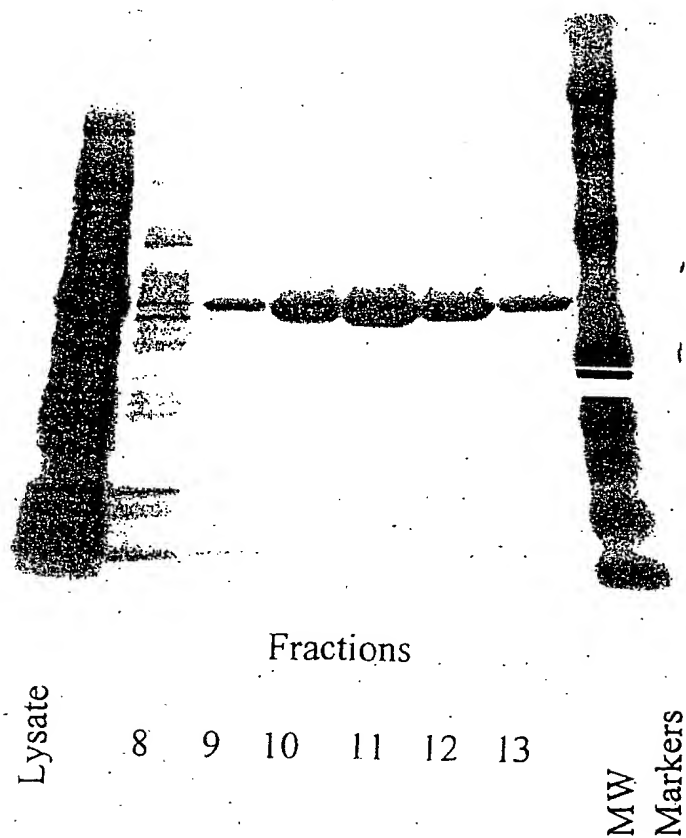


FIGURE 21

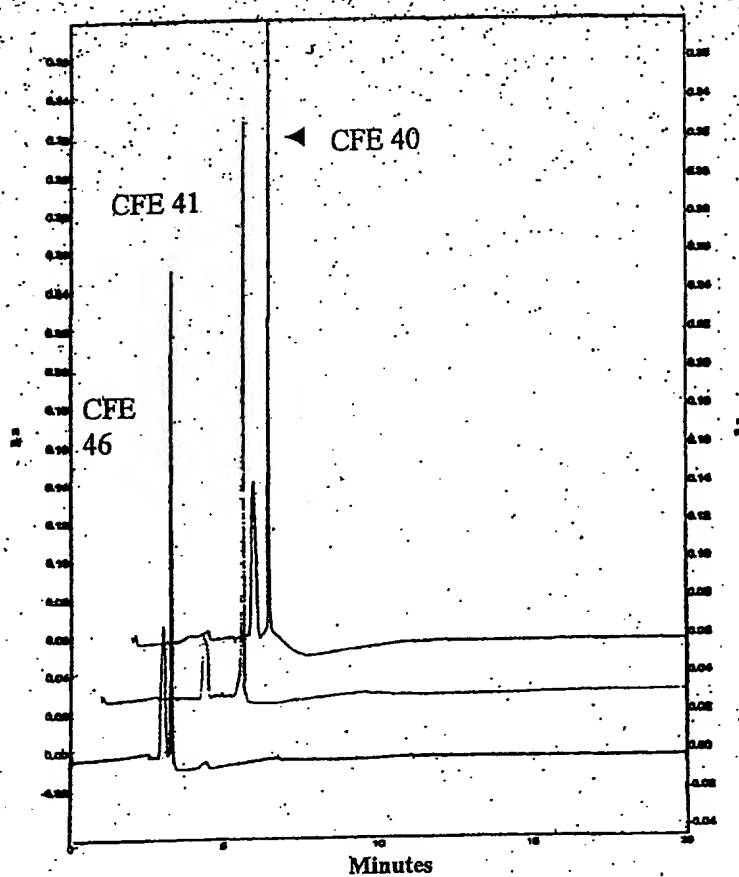


FIGURE 22



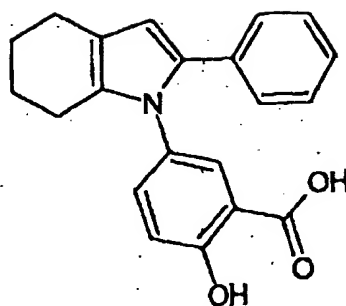


FIGURE 23

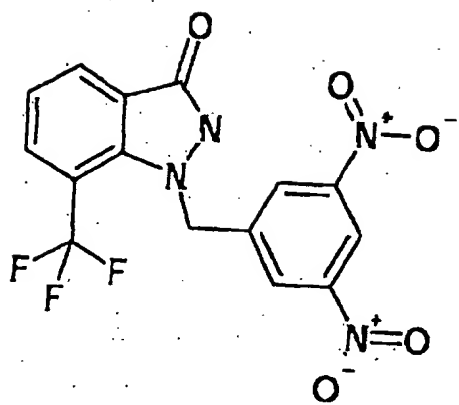


FIGURE 24

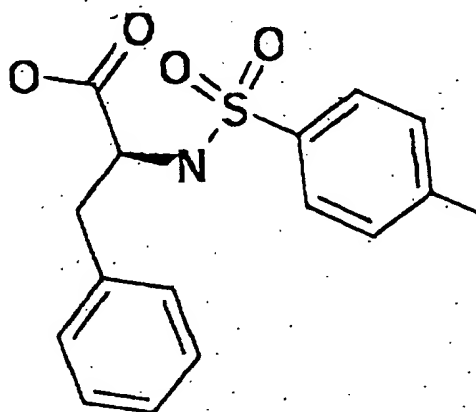


FIGURE 25

2 CFE1 "homologue of SEQ. ID NO. 1"

ATGATTATGCGAATTCCTTGCCGGTGGAACTGGCACACGCATGGGGATCAGTAACCTGCCAAAACAAT  
 TTITAGAGCTAGGTGATCGACCTATTTGATTTCATACAATTGAAAAATTNGTCTTGGAGCCAAGTATTGAA  
 AAAATTGTAGTTGGTGTTCATGGAGACTGGGTTTCTCATGCAGAAAGATCTTGTAGATAAATATCTTCTCT  
 TTATAAGGAACGTATCATCATTACAAAGGGTGGTGTGACCGCAATACAAGTATTAAGAACATCATTGAA  
 GCCATTGATGCTTATCGTCCGCTTACTCCAGAGGATATCGTTGTTACCCACGATTCTGTTCTGTTCCATTATT  
 ACACCTTCCATGATTACAGGACAATATCCAACCTTGCCCAAAATCATGACGCAGTGGACACAGTGGTAGAA  
 GCGGTTGATACTATCGTTGAAAGTACCAATGOTCAATTTATTACAGATATTCCAAATCGTGCTCACCTTTA  
 TCAAGGACAAACACCTCAAAACATTCCGTTGCAAGGACTTCATGGACCTTTATGGATCTCTTTCTGATGAA  
 GAGAAAGAAATCTTGACAGATGCATGTAAATCTTTGTGATCAAAGGAAAAGATGTGGCTTTGCCAAA  
 GGTGAATACTCAAATCTGAAGATTACAACCGTAACAGATTGGAAGATTGCAAAAAGTATGATTGAQAAA  
 GACTAG

2 CFE2 "homologue of SEQ. ID NO. 2"

ATGGCTAACGTAATTATTGAAAAAGATAAAAAGAGAGAATGACCCATCTCACCAATCACTTGCTCGTGAAT  
 TTGGTGTATCCGTGCTGGTCTGTCGCAATGCAAGCTTGCTTGACCGTGTACATGTAGAATACTATGGAGTC  
 GAAACTCTCTTAACCAAATCGCTTCAATTACGATTCCAGAAGCGCGTGTGTTGTTGGTAACACCAATTTGA  
 CAAGTCTTCATTGAAAGACATCGACCGTGCTTGAACGCTTCTGATCTTGGTATCACACCGGCTAATGAC  
 GGTCTGTGATTCGCTTGTATCCAGCTCTTACAGAAGAAACTCGTCTGTGACCTTGCTAAAAGAAAGTGA  
 AGAAGGTCGGGAAAATGCTAAAGTGGCTGTCCGCAATATCCGTGCGCATGCTATGGACGAAGCTAAGA  
 AACAAAGAAAAGCAAAAGAAATCACTGAAGACGAATTGAAGACTCTTGAAAAAGATATTCAAAAAGTA  
 ACAGACGATGTGTAAACACATCGACGACATGACTGCTAACAAAGAGAAAAGAACTTTTGGAAAGTCTAA

2 CFE3 "homologue of SEQ. ID NO. 3"

ATGGGTAAATATTTGGGACTGATGGAGTCCGTGGAGAAGCTAACCTAGAGCTAACACCAGAATTAGCCT  
 TTAAACTAGGACGTTTGGAGGCTATGTTCTTAGTCAACATGAAACGGAAGCCCGAAAAGTCTTTGTAGG  
 ACCTGACACACGTATTTACGGGGAATGCTGGAATCGGCCTTGGTGGCAGGTCTCTTTCAGTAGGGATT  
 CAGGTATACAAACTTGGTGTCTTGCACACCCAGCAGTAGCTTACTTGGTTGAAACTGAAGGAGCAAGTG  
 CCGGTGTCATGATTTCTGTAGCCACAACCCAGCCCTTGATAACGGAATCAAGTCTTTGCGGGTGTAGG  
 CTTCAACTAGATGATGAAAAAGAGCAGAAATGAAGCCTTGCTAGATGCTGAGGAAGACACTCTTCC  
 TCGTCCAAGTGCAGAAAGGCTTAGGAATTTGGTAGATTATCCAGAAGGCTTGCGTAAGTATGAAGGATAC  
 CTGTGTTCAACTGGAACTCCTTGTATGGAATGAAGGTTGCTTGGATACAGCTAATGGAGCAGCTTCTAC  
 CAGTGGCGGTCAAATCTTTGCAGACCTTGGTGCCCAATTGACGGTTATCGGGGAAACACCAAGACGGTCTT  
 AAGATCAACCTTAATGTTGGTTCAACACATCCAGAAGCCCTTCAAGAAAGTGGTCAAAGAAAGTGGGTCA  
 GCTATGTTTGGGCTTTGATGGAGACAGTGACCGCTTGATTGCTGTTGATGAGAATGGTGACATCGTCC  
 ATGGTGCAAGATTATGTACATCATCGGAAAATACCTTTCTAAAAAAGGACAATTGGCTCAAAATACAAT  
 TGTGACAACCTGTTATGTCTAACCTTGGTTCCACAAGGCCTTGAATCGCGAAGGTATTAACAAGGCAGTT  
 ACTGCAGTTGGTGACCGCTACGTTGTTGAAGAAATGAGAAAAATCAGGTTACAACCTTGGTGGTGAACAGT  
 CTGGTCACGTTATCTGATGGATTACAATACCACAGGTGATGGTCAATTAATCAGCAGTTCAATTGACTAA  
 AATCATGAAGGAACTGGTAAGAGCTTATCAGAGTTGGCGGCAGAAAGTAACGATTATCCACAAAAT  
 AGTTAATATCCGAGTGGAAAACGTCATGAAGGAAAAGGCCATGGAAGTCCAGCTATCAAGGCCATCAT  
 CGAGAAATGGAAGAAAGAAATGGCGGGAAACGGCCGTATCCTTGTTCGTCCAAGTGGAAACAGAACCCCT  
 CTTCGGTGTATGGCAGAAGCGCCTACAACAAGAAAGTAGACTACTATGTTGATACCATCACAGATGTA  
 GTTCGTGCTGAAATTTGGGATTGACTAA

2 CFE4 "homologue of SEQ. ID NO. 4"

2CFE 4 homologue of SEQ ID NO: 4

Fig. 29  
 ATGAAAAAATACTAATTGTAGATGATGAGAAACCAATCTCGGATATTATCAAGTTTAAATGACCAAGG  
 AAGGTTATGAAGTTGTAAGTCTTTAATGGTGGTGAAGCGCTAGAGCAATTTGAAGCAGAGCAACCAGA  
 TATTATTCTCTGGATTGATGCTTCCAGAAATGATGGTTTGAAGTTGCTAAGACCATTCGTAAAGACAA  
 GCAATGCCCCATTCTTATGCTTTCAGCCAAAGATAGTGAATTTGATAAGGTTATCGGTTTGGAACTTGGG  
 GCAGATGACTATGTAACGAAACCCCTTCTCCAATCGTGAGTTGCAGGCGCGTGTAAAGCTCTTCTGCGTC  
 GTTCTCAACCTATGCCAGTAGATGGTCAGGAAGCAGATAGTAAACCTCAACCTATCCAAATTGGGGATTT  
 AGAAATTGTTCCAGACGCTACGTGGCTAAAAAATATGCCGAAGAACTAGACTTAACCCATCGTGAAATTT  
 GAGCTTTGTATCATTTAGCACCGCATACAGGTCAAGTCATCACGCGGAAACACTTGCTTGAGACTGTCT  
 GGGGTTATGACTATTTTGGTGATGTCCGCACAGTTGATGTGACTGTACGACGTCTGCGTGAGAAGATTGA  
 AGATAAGCCGAGCCGACCAGATATATCTTGACGCGCGTGGTGTAGGGTATTACATGAGAAATAATGCT  
 TCA

2CFE 5 "homologue of SEQ. ID NO. 5"

Fig. 30  
 ATGGAAGAAATTTCTGTATTGGTTGTGGAGCAACCATTTCAGACGACAGATAAGGCTGGTCTTGGTTTTA  
 CCCCCAGTTGGCACTTGAAAAAGGTTTGGAGACTGGCGAAGTCTATTGCCAACGCTGTTCCGTCCTCCG  
 CCACTCAATGAAATCACAGATGTCCAGTTGACGGACGATGATTTCCTCAAGCTCTTGCACGAGGTGGGA  
 QACAGTGATGCTTTAGTGGTCAATGTCAATTGATATCTTTGATTTAATGGATCTGTATCCAGGTTTACC  
 ACGTTTTCGTCGCGGCAATGATGTCTCTTGGTAGGAAATAAAAAAGATATCCTTCTAAGTCAGTTAAG  
 TGTGTAAGATTAGCCAGTGGCTCATGAAACGTGCCCATGAAGAAAGGTTCTTCGTCAGTGCATGTGTCTC  
 TAACCTTCAGCACAAATAAATATGCCATTAAAGGAATCATGATAAGATTGAACACTACCGTAAGGGGCC  
 GCGATGTCTATGTGGTGGTGTGACCAACGTGTGAAATCAACTCTAATCAATGCTATTATCCAAGAAAT  
 CACGGGTGATCAGAATGTCACTACTTACGCTTTCAGGGACAACCTTGGACAAAATAGAGATTTCGG  
 CTGACACGCGATCTTATATTACGATACGCGGGAATTATCCACCGCCACCAGATGGCTCACTACTTGA  
 CGGCAAAAACCTCAAGTATGTCACTCTAAAAAGGAAATCAAGCCTAAGACCTATCAGCTTAATCTGTA  
 GCAAAACCTATTATTTAGGTGGTTTGGGACGCTTGACTTTATAGCAGGAGAAAAAGCAAGGATTTACTGCT  
 TTCTTTGATAATGAACCTCAAACTCCATCCTAGCAAGCTTGAAGGAGCTAGTGCTTTCTACGATAAGCACC  
 TGGAACTCTTCTGACACCACCAAAATAGCAAGGAAAAAGAGATTTCCTCAAGGCTAGTCCAGCATGTCTT  
 TACCATTAAAGATAAGACAGACCTAGTCATTTCAAGGCTAGGCTGGATTCTGTAAACAGGCATAGCAAAA  
 GTCCGCTCTGGGCACCAGAAGGCGTCCGCTCGTCAACGAAAAAGCAATTATTTAA

2CFE 6 "homologue of SEQ. ID NO. 6"

Fig. 31  
 ATGTATCAGATGATAGTTTGACATTGCACACGGACTTGTACCAGATCAACATGATGCAGGTTTACTTTO  
 ACCAAGGGATTACAAATAAGAAAGCGGCTTTTGGAGGTGATTTCCGCCAACAGCCTTTTAAAGAACGGCTA  
 TGGGTTTGTGAGGTTTGGAAAGAATTGTGAACATCTTGAAGACTTGGGTTTTCAGATAGTGATATAG  
 CCTATTGGAGTCGCTTGGTTATCATGGGGCGTCTTGGATTACCTTCGCAATTTCAAGTTGGAGTTGACC  
 GTTCGTTCTGCCAAGAAGGGGATTGGTTTGTGTAATGAACCGATTGTGCAGGTGGAAGGACCTCTAG  
 CCAATGTCAGTTGGTCGAAACGGCTCTTTGAACATCGTCAACTACCAGACCTTGGTGGCGGAGAGGC  
 AGCTCGATTGCTTGGTTATCGAAGATGAACCTTGTATGGAATTTGGGACACGTGGGGCTCAAGAAATG  
 GATGCCGCCATCTGGGGAACACGGCAGCTGTGATTGGTGGCGCAATGGAAACAGCAACGTGCTGCG  
 GGTAAAGCTCTTTGACATTCTGTTTTGGGAACCCATGCCATGCCTTGGTACAGGTTTATGGCAATGACTA  
 TGAAGCTTTCAAGGCTTACGCTGCGACCCACAAAAATTTGTCTTCTTGTGATACCTATGACACCCCTC  
 GATCGGTGTACAGCTGCCATTTCAGGTGGCGCGTGAGCTGGGTGATTAGATTAACTTTATGGGTGTGCG  
 GATTGACTCTGGGATATTGCTACATTTCTAAGAAAGTCCGTCAGCAACTGGACGAGGCTGGATTTACA  
 GAGGCTAAGATTATGCTTCTAATGATTTGGACGAAAAATACTATCCTCAACCTCAAGATGCAAAAAGGCCA  
 AGATTGATGTCTGGGGCGTGGGTACCAAGCTGATTACAGCCTATGACCAGCCAGCTCTTGGGGCGGTTTA  
 CAAGATTGTTGCAATCGAAGATGAAACTGGTCAGATGCGCAATACGATTAAGCTGTCTAATAATGCGGA  
 AAAAGTGTCCAGCCAGGTAAGAAAGCAGGTGTGGCGCATACCAAGTCTGAAAAAGGCAAGTCAGAAG  
 GTGACTACATCACTTATGATGGTGTGGATATTAGCGACATGACAGAAATCAAGATGTTCCATCCGACCTA  
 TACATACTCAAGAAAGCGGTCGTAATTTTGTATGCCGTTCTCTCTTGGTGGATATCTTCAAGAAAGGTA  
 TATTAAGTTACAACTGCTAGTTGACTGACATTCAGGATTATGCCCGTAAGGAATTTGACAAAGTTGTGG  
 GATGAGTATAAGCGTGTGCTCAATCCGCAGCACTATCCAGTGGATTGGCGCGTGATGTATGGCAAGATA  
 AGATGGACTTGTGATAAGATGCGCAAGGAAGCCCTTGGTGAAGGAGAAGAAAGTA

2CFE 7 "homologue of SEQ. ID NO. 7"

Fig. 32  
 ATGGCTACTATTCAATGGTTTCTGGTCACATGTCTAAAGCGCGTCGACAGGTGCAGGAAAAATTTAAAT  
 TTGTTGATTTTGTGACGATTTTATAGATGCACGCTTGCCTCTATCTAGTCAAAATCCTATGTTGACCAAG

2CFE 7 (contd)

Fig 32 (contd)

ATTGTTGGTGATAAAACCAAACTCTTGTATTTTAAACAAGGCCGACTTGGCTGATCCAGCAATGACCAAGG  
 AATGGCGTCAGTATTTTGAATCACAAGGAATCEAGACGCTAGCTATCAACTCCAAAGAGCAAGTGACTGT  
 AAAAGTGTAAACAGATGCGGCCAAGAAGCTCATGGCTGATAAGATTGCTCGCCAGAAAGAACGTGGGAT  
 TCAGATTGAAACCTTGGTACCATGATTATCGGGATTCCAAACGCTGGTAAATCCACTCTGATGAACCGT  
 TTGGCTGGTAAAAAGATTGCTGTTGTTGGAAACAAGCCAGGGGTACAAAAAGGTCAACAATGGCTTAAA  
 ACCAAATAAGATCTGGAAATCTTGGATACACCGGGGATTCTCTGGCCTAAGTTTQAGGATGAAACTGTTQ  
 CACTTAAGTTGGCATTGACTGGAGCTATCAAGGATCAGTTGCTTCCATGAGATGAGGTTACCATTTTTGGT  
 ATCAATATTTCAAAGAACATTATCCAGAAAAGCTGGCTGAACGGCTTCAAACAAATGAAAAATTGAAGAA  
 GAAGCCCTGTGATTATTATAGATATGACCCGCGCCCTCGGTTTCCGTGATGACTATGACCGTTTITACAG  
 TCTGTTGTGAAGGAAGTCCGTGATGGCAAACTCGGTAACCTATACCTTAGATACATTGGAAGACCTCGAT  
 GGCAAGATTAA

Fig 33

2CFE8 "homologue of SEQ. ID NO. 8"

ATDATTACAATGTTTACTTGTAGGGCGTATGACACGTGACGCTGAGTTGCGTTATACCCCATCAAAATG  
 TAGCAGTTGGCAGCTTTACTCTTGCAGTAAACCGTACATTTAAGAGTCAAAATGGTGAACGTGAGGCTGA  
 TTTATCAATGTCGTTATGTGGCGCCAAACAGGCTGAAAAATCTTGTAACTGGGCTAAAAAGGCTCACTT  
 ATCGGGGTGACAGGTCGTATCCAGACTCGTAGTTACGATAACCAGCAAGGACAACGTGTCTACGTGACA  
 CAGGTGCTGGCTGAGAAATTTCCAAATGTTGGAAAGCCGTAGTGTGCGTGAGGGTCACACAGGTGGAGCT  
 TACTCTGACCAACTGCAAACTATTACGACCTACAAATTCAGTACCAAGACTTTTACGTAATGAAAAATC  
 CATTTGAGCAACAAACCCATTGATATTTAGATGATGATTACCATTTCTAA

Fig 34

2CFE9 "homologue of SEQ. ID NO. 9"

ATGAAAACGGCTATTACAGAATTATTGAAGATTGACTATCCTATTTTCCAAGGAGGGATGGCTGGGTTG  
 CTGATGTTGATTTGGCAGGGGCTGTTTCCAAGGCTGGAGGATTAGGAATTATCGGTGGGGGAAATGCCCC  
 GAAAGAAGTTGTCAAGGCCAATATTGATAAAATCAAATCATTGACTGATAAAACCCCTTTGGGGTCAACATC  
 ATGCTCTTATCTCCCTTTGTGGAAGATATCGTGGATCTCGTTATTGAAGAAGGTGTTAAAGTTGTCAACAC  
 AGGAGCGAGAAATCCAAGCAAGTATATGGAACGTTTCCATGAAAGCTGGGATAATCGTTATTCCTGTGCTT  
 CCTATTTGCGGTTTAGCTAAACCGCATGGAAAAAATCGGTGCGAGCGCTGTTATTGCAGAAGGAATGAAA  
 GCTGGGGGGCATATCGGTAAATTAACAACCATGACCTTGGTGGCAGAGGTAGCCACAGCTGTATCTATTTC  
 CTGTTATTGCTGCGAGGAGAAATGGCGGATGGTGAAGGTGCTGGCGCTGGCTTTATGCTAGGTGAGAGGC  
 TGTACAGGTGGGGACACGGTTTGTAGTTGCAAAAAGAGTCGAATGCCATCCAACTACAAGGAGAAAAAT  
 TTAAAAAGCAAGGGAATTTGACACTACGATTTAGCTCAGCACCTTTGGTCACTGCTGTTCTGCTATTAAAA  
 ATCAGTTGACTAGAGATTTTGAAGTGGCTGAAAAAGATGCCCTTAAGCAGGAAGATCCTGATTTAGAAAT  
 CTITGAACAAATGGGAGCAGGTGCCCTAGCCAAAGCAGTTGTTACCGGTGATGTGGAGGGTGGCTCTGTC  
 ATGGCAGGTCAAAATCGCAGGGCTTGTCTTAAAGAAAGAACAGCTGAAGAAATCCTAAAAAGATTGTATT  
 ACCGAGCCGCTAAGAAAATTCAGAAGGAAGCCTCTCGCTGGACAGGAGTTGTAAGAAATGACTAA

Fig 35

2CFE10 "homologue of SEQ. ID NO. 10"

ATGATCQATATTCAAGGAATCAAAGAAGCTCTTCCCCACCGTTATCCTATGCTTCTAGTGGACCGTGTCTT  
 GGAAGTGAGCGAGGATACCATTTGTTGCTATCAAAAAATGTGACCATTAACGAACCTTTCTTAAACGGCCAC  
 TTCTCTCAATACCCAGTTATGCCAGGTGTTCTGATTATGGAAGCCTTGGGCAAACTGCTGGTGTGTTGGA  
 GTTATCAAAACCTGAAAAATAAGGAAAACTGGTCTTTACGCTGGTATGGACAAGGTTAAGTTCAAGAA  
 GCAAGTTGTACAGGGCAACCAATTGGTTATGACAGCGACTTTTGTAAAAACGTCGTGGCACCATAAGCTGTG  
 GTTGAACCAAAAGGCTGAAGTGGATGGCAAGCTTGCAGCCAGTGTATCCTTACTTTTCAATTGGGAACT  
 AA

Fig 36

2CFE11 "homologue of SEQ. ID NO. 11"

ATGATTATCAAATTTATCAACTAAGCCTAAGTTTATCAATGTCAAATATCAGGAAGAGGCTATTG  
 ACCAAGAGAAATCATATCCTTATCCGTCCCAACTACATGGCTGTCTGTATGCGGATCAGCGTTACTATCA  
 GGAAGAACGTGATCCCAAGATTTGAATAAAAAGCTTCCAATGGCAATGATTCACGAGTCATGTGGAAC  
 CGTCAATTCTGACCCGACCGGAACCTACGAGGTTGTGTCAAAAAGTTGTCATGATTECCAATCAGTCTCT  
 ATGACAGATGATGAAGAAATCTATGAAAACTACATGACAGGGACCCATTCTTGTCTAGTGGATTGATG  
 GCTTATAGAGAGTTTGTCTCTCCCTAAAGATCGTGTGGTGGCTTATGATGCTATTGAAGATACGGTT  
 GCAGGCATTACAGATTTGTGAGTGTGGGCATGCACGCTATGAATCGTCTATTGACTCTGTCTATGCA  
 AGCGGGAGCGGATCGCCGTTATTGGAGATGGAAGTTTACGTTTGTGGTTGCCAATATTATEAACTATAC  
 TTGCAAGAAAGCAGAGATTGTGGTTATTGGTCTATTGGGAAAAGTTGGAACCTCTCTCATTTGCCAAA

Fig. 36 (contd.)

## 2 CFE 11 (contd.)

GAATGCTATATTACGGATAATATTCCTGAAGATTGGCCCTTTGACCATGCTTTGAATGTTGTGGTGGTGA  
TGGTACTGGACCAGCTATTAATGACTGTGATTCGCTACATTGCTCCTCAGGGAACGATTCTCATGATGGGA  
GTTAGCGAATATAAAGTCAATCTCAATACTCGCGATGCTTAGAAAAAGGCTTGATTTGGGTTGGGTCAT  
CTCGTTCTGGTCCGATTGATTTTGAAAAATGCTATCCAAATGATGGAAGTCAAGAAATTTGCCAATCGTCTT  
AAAAATATCCTTTATCTAGAAGAAOCTGTAAGAGAAATIAAAGATATTCATCGTGTCTTTGCAACCGATT  
TAAACACAGCCTTTAAAAACAGTGTTTAAGTGGGAAGTATAA

Fig. 37

## 2 CFE12 "homologue of SEQ. ID NO. 12"

ATGAACITAAAACTACTTTGGGCCCTTCTTGCTGGGCGTCTCTCCCACTTCGTTTTAAGCCGCTTTGGACG  
TGAAAGTACGCTCCCAAGGAAAGTCGCCCTTCAATTTGATAAAAGATATTTACAAAGCCTAGCTAAGAA  
TACGAGATTGTGCTGCTCACTGGAACAAATGGAAAAACCCGACAACTGCCCTCACTGTGCGGCTTTTAA  
AAGAGCTTTATGGTCAAGTTCTAACCAACCCAAAGCGGTGCCAACATGATTACAGGGATTGCAACAACCTT  
CCTAACAGCCAAATCTTCAAAAACCTGGGAAAAATATTGCCGCTCCTCGAAATGACGAAGCCAGTCTATCT  
CGTATCTGTGACTATATCCAGCCTAGTCTTTTGTCACTACTAATATCTCCGCTGACCCAGATGGACCGTTTC  
CGTGAAATCTATATACTAACCATAACATGATATTGGATGCCATTGCAAAAGTTCCAACTGCTACTGTTCTCCT  
TAACGGAGACAGTCCAETTTTCTACAAGCCAACTATTCCAAACCCCTATAGAGTATTTGGTTTTGACTTGG  
AAAAAGGACGAGCCCAACTGGCTCACTACAATACCGAAGGGATTCCTGTGCTGACTGCCAAGGCATCCT  
CAATATGAGCATAATACCTATGCAAACTTGGGTGCTATATCTGTGAAGGTTGTGGATGTAAACGCTCT  
GATCTGACTATCGTTTGACAAAACCTGTTGAGTTGACCAACAATCGCTCTCGCTTTGTCATAGACGGCC  
AAGAATACGGTATCCAAATCGGCGGGCTCTATAATATCTATAACGCCCTAGCTGCTGTGGCCATCGCCCG  
TTTCTAGGTGCGGATTCCGCAACTCATCAAAACAGGGATTGACAAGAGCCGCTGTCTTTGGACGCCAA  
GAAACCTTTCTATCGGTGACAAGGAATGTACCCTTGTCTTGATTAAAAATCCAGTCCGGTGCAACCCAA  
CTATCGAAATGATCAAACTAGCACCTTATCCATTTAGCCTATCTGTCTCTCTAATGCCAACTATGCAGAT  
GGAATGACACTAGCTGGATCTGGGATGCAGACTTTGAACAAATCACTGACATGGACATTCCTGAAATCA  
ACGCTGCGGCTGTTCTGTCATTCTGAAATCGCTCGCTCGCCTCCGAGTGACTGGCTATCCAGCTGAGAAAA  
CACTGAAACGAGTAATCTGGAGCAAGTTCTCAAGACCATTGAGAATCAAGACTGCAAGCATGCCTATATT  
CTGGCACTTATATCTGCCATGCTGGAATTTCTGTGAAGTGTGCTAGTCTGTCAGATTGTTAGAAAGGAGA  
TGAACCTAA

Fig. 38

## 2 CFE13 "homologue of SEQ. ID NO. 13"

ATGTTTATACTTCACTTTCTCCTCAAAAGATGGCAATTACCCCTATCAGCTCAACATTGCCACCTCTACGG  
AAATCTGATGAATACCTACGGGGACAATGGAAACATCCTCATGCTCAAGTATGTGGCTGAAAACTGGG  
AGCCCAATGTGACCGTTGACATCGTTTCTGCTCATGATGACTTTGATGAAAAATCACTACGACATCGCCTTTT  
TCGCTGCTGGTCAAGACTTTGAACAAAGTATCATTTGCAGACGACCTACCTGCTAAAAAAGAGAGCATTG  
ACAACATCATCCAAAAAGCAGCGGTGATGTTCTGGCTATCTGCGGTGGTTTCCAACTATTGGGTCAATATTAT  
GTTGAAGCTTTCAGGAAAAACGTATCGAAGGGCTAGGGGTGATGGGACACTACAGCTCAACCAGACCAAT  
AACCGTTTATCGGTGACATCAAGATTCAAAATGAAGATTTCGATGAAACCTACTATGGATTGAAAAATC  
ACCAAGGCCGTACCTTCTCTGATGACCAAAAAACCGCTGGGACAGGTTGCTATGGAAATGGAAACAA  
CGAAGAAAAAGGTGGTGAAGGGGTTCAATTAAGAATGTCTTTGGTTCTACTTCCACGGGCCCTATCTC  
TCTCGTAATGCCAATCTGGCTTATCGCCTAGTTACTACTGCCCTCAAGAAGAAATATGGTCAGGACATCC  
AATCTCTGCCATGAGGATATCCTCAGCCAAGAAATCGCTGAAGAGTACAGTGACGTCAAAAGCAAGG  
CTGACTTTTCTAA

Fig. 39

## 2 CFE14

ATGAATGTAAAAAGAAATACAGAACTTGTTTTTCGAGAAGTTGCAGAGGCTAGTCTGAGTGTCTCATCGAG  
AGAATGCTTCCGTCTCTGTCAATTGCAGTTATCAAGTATGTAGATGTACCGACAGCGGAAGCCTTCTTCC  
GCTAGGTGTTTCATATATCGGTGAAAAATCGTGTAGATAAGTTTCTGGAAAAATATGAAGCTTTAAAAGAT  
CGAGATCTGACTGGCATTGATTGGTACCTTCCAAAGACGTAAGGTGAAAAATGTCAATTCAATACGTTG  
ATTATTTCATGCTATTGGACTCAGTAAAGCTAGCAGGGGAAATTCAAAAAGAAAGTGACCGAGTCATCA  
AGTGTCTTCTCAAGTAAATATTCTAAAGAAGAAACCAACACCGTTTTCGAGAGAGGAACTGCTGGA  
AATCTTGCCAGAGTTAGCCAGACTAGATAAGATTGAATATGTTGGTTAATGACGATGGCACCTTTTGAG  
GCTAGCAGTGACGAGTTGAAAGAGATTTTCAAGGCGGGCCCAAGATTACAAAGAGAAATTCAGAGAAA  
CAATTCCAAATATGCCATGACCGAGTTAAGTATGGGAATGAGTCGTGATTATAAAGAAAGCGATTCAAT  
TCGTTTCACTTTTGTTCGTATAGGTACATCATTTTAAAGTAG

## 2CFE15 "homologue of SEQ. ID NO. 15"

ATGGGAATTGCTCTAGAAAATGTGAATTTATATATCAAGAAGGTACTCCCTTAGCTTCAGCAGCTTTGTC  
GGATGTTCTTTGACGATTGAAGATGGCTCTTATACAGCTTTAATTGGGCACACAGGTAGTGGTAAATCA  
ACTATTTTACAACTCTTAAATGGTTTATTGGTGCCAAAGTCAAGGGAGTGTGAGGGTTTTTGATACCTTAAT  
CACTGACCTCTAAAAATAAAGATATTGCTCAAATTAGAAAACAGGTTGGCTTGGTATTTCAGTTTGGCT  
GAAAATCAGATTTTTGAAGAAACGGTTTTGAAGGACGTTGCTTTTTGGACCGCAAAATTTGGAGTTTCTG  
AAGAGATGCTGTGAAGACTGCGCGTGAGAAAAGTGGCTGCTGGTTGGAATTGATGAATCACTTTTGTATCG  
TAGTCCGTTTGGCTGTGAGGGGGACAAATGAGACGTTGCCATTGCAGGCATACCTGCCATGGAGCCA  
TGTATATTAGTCTTAGATGAGCCAACAGCTGGTCTAGATCCTCTAGGGAGAAAAGAGTTGATGACCTGT  
TCAAAAACCTCCACCAGTCAGGGATGACCATCGTCTTGGTAACGCATTGATGGATGATGTTGCTGAATA  
TCTAAATCAAGTCTATGTAATGGAAGGGGACGTTAGTAAAGGGGGGCAACCAAGTATGCTTTCA  
AGACCTGTTTTATGGAAGAAAGTTCAAGTTGGGAGTACGTAAAAATTACGGCCTTTTGTAAACGATTGGCT  
GATAGAGGCGTGTCAATTAACGATTACCGATTAAAGATAGAGGAGTTCAAGGATCGCTAAATGGATAG

## 2CFE16 "homologue of SEQ. ID NO. 16"

ATGGATATTCAATTTTTAGGAACGGGGGCTGGTCAGCCCTCTAAAGCCCGCAACGTTTCAAGTCTCGCCC  
TGAACCTCTTGGATGAGATTAACGAAGTTTGGCTCTTTGACTGTGGAGAAAGGTACGCAAAATCGCATTCT  
CGAAGCACAATTCGACCAGTAAGGTCAGCAAAATCTTTATTACCATCTGCATGGAGACCACATTTT  
CGTTTCCAGGTTTCTTTCTAGCCGTGCTTTTACGGCCAATGAAGAGCAGACAGATTGGGAAATCTACG  
GACCTCAAGGAATCAAGTCATTTGTCTTAACCAAGCCTTCGTGTGTCAGGTTCTCGTCTGCCCTACCGCATT  
CAATTTCTATGAOTTTGACCAAGATTCTCTGGGTAAAAATCTTGAACCGATAAAATTCACCTGTGTATGCAGA  
GGAGCTGGACCACTATTTTCTGTGTTGGCTATCGTGTATGCAAAAGGATCTAGAAGGGAGCGTGGAT  
CGTGAATAACTCAAGGCTGCTGGTGTCCGTTCCGCCCGCTTTTGGTAAAAATCAAAAACGGCCAGGATC  
TTGTTTGGAAAGACGGAACTGAAATCAAGGCAGCAGACTATATCTCAGCGCCACGTCCAGTCAAGATTAT  
CACTATTTAGGAGACACTCGAAAAACGGGTGCCAOTGTGCGTCTGCTGTCAATGCAGATGTCTAGTT  
CATGAGTCCAATTATGGCAAGGGTGTGAAAAAATGCTCGTAACCATGGTCACTCAACTAATATGCAAG  
CTGCAGAAATAGCGGTAGAAAGCAGGTGCCAAACGCTCTACTCAACCATATCAAGTCCCGTTTCTCTCTC  
AAAAGATATTAGCAAACTCAAGAAAGACGCTGCCACAAATTTTGAAAAATGTCCATGTGGTCAAAAGACTTG  
GAAGAAGTGGAAATCTAG

## 2CFE17 "homologue of SEQ. ID NO. 17"

ATGAGTAATATCAGTTTAAACAACACTTGGTGGTGTGCGTGAGAATGAAAAAATATGTACATTGCTGAAA  
TTGGAGAGTCCATTTTGTTTGAATGTAGGGTTAAATATCTCGAAAAATGAACAATTAAGGGGTCGATGT  
GGTGATTCCAAACATGGATTACCTTTTGAATAAGCGACCGTATTGCTGGGGTTTCTTGACCCACGGGC  
ATGCGGATGCCATTGGTGTCTACCTTATCTCTTGGCAGAGGCTAAAGTTCTGTATTGGGTCTGAGTTG  
ACCATTCAGTTGGCAAAGCTCTTTGTCAAAGGAAATGATGCCGTTAAGAAATTTAATGATTTCCATGTCA  
TTGATGAGAATACGGAGATTGATTTGGTGGGACAGTGGTTTCTTCTTCCCTACGACTTACTCCGTTCCA  
GAGATCTGGGAATTTGTCTTGAAGACATCGGAAGGAAGCATCGTTTATACAGGTGACTTCAAATTTGACC  
AAACCGCTAGTGAATCTTATGCAACTGATTTTGTCTGTTTGGCAGAGATTGGTCGTGACCGCGTCTGGC  
TCTCTCAGTGATTGGGCCAATGCAGACAGCAATATTACGGTGGCTAGTGAAAGTGAAGTTAGGGATGAA  
ATTACCCAAACTATTGCTGACTGGGAAGGTGATCATCGTTGCAGCTGTTTCCAGTAATCTTTCTCGTAT  
TGAAGCAATTTTACCGCTGCGGATAAAACAGGTGACGATCGTCTTGACAGGATTGATATTGAAAAT  
ATGCTCCGACAGCGATTCTGCTTAAGAAGTTGTGTTAGCCAAACGAAATTTCTTTGATTAAAGCCTAAAG  
ATATGCTCTCGCTTGAAGACCATGAGTTGATTATCTTGAACAGGTGATGGGTGAACCTATCAATGG  
AGTTGCTAAGATGTCGATTGGTCCCATCGTTATGTAGAAATCAAGGATGGGGACCTGCTATATTGCT  
ACCGCTCCGTCTATTGCTAAAGAACCTTTGTTGCGCGTGTGGAAAAATATGATTTATCAGGCAGGTGGGG  
TTGTGAAATTTGATTACCCAAAGTTTACATGTATCAGGGCACGGAAATGTGCGTGATTGTCAGCTGATGAT  
CAATCTTTTGCAACCTAAGTACCTCTTCCCTGTCCAAGGGGAGTATCGTGAGTTGGATGCTCACGCTAAG  
GCTCCCATGGCAAGTTGGGATGTTGCCAGAACGCATCTTCATTCTTAAAGGGGACGACCATGGCTTACG  
AGATGTCAGACTTTGTTCCAGCTGATCGGTTTTCAGCAGGAGATATCTTGATGATGGGAATGCCATTGG  
TGATGTTGAAATGTTGTTCTTCTGACCGTAAGGTCTTGTGACAGGATGGAATTTTCATCGTGGCTATA  
CAGTCAACCGTCTGTGAGAAGAAATTTGTGGCTAGAGCTGTTGTCAGACCGGTGGATTTGTTATCTTAA  
GAAGAGTCCGCTATTTCTCCGTGAAAGTTTCAAGTTGATTAAACCAACCGGTAGAAGAGTATCTTCAAGG  
AGATGACTTTGACTGGGCAGATCTCAAGGTAAGGTTCTGTGACAAATCTGACCAAGTACCTCTTTGATCAA  
ACCAAGGCTCGCCAGCCATTTTACAGTAGTCATGGAAGCAAAATAA



## 2 CFE19 "homologue of SEQ. ID NO. 18"

ATGACAAAAGAAATTCATCATGTAACGGTCTTACTCCACGAAACGATTGATATGCTTGACGTAAAGCCTG  
 AAGGTATCTACGTTGATGCGACTTTGGGCGGAGCAGGACATAGCGAGTATTTATTAAGTAAATTAAGTGA  
 AAAAGGCCATCTCTATGCCTTTGACCAGGATCAGAATGCCATTGACAATGCGCAAAAAAGCTTGGCACCT  
 TACATTGAGAAGGGAATGGTGACCTTTATCAAGGATAAATCTCCGTCAATTTACAGGCACGTTTGGCGGAAG  
 CTGGTGTTCAGGAAATTTGATGGAATTTGTTATGACTTGGGAGTGTCTAGTCCCTCAATTGGACCAGCGTGA  
 GCGTGTCTTTCTTATAAAAAAGGATGCGCCACTGGACATGCGGATGAATCAGGATGCTAGTCTGACAGCC  
 TATGAAAGTGGTTAATCATTATGACTATCATGATTTGGTTCGTATTTCTTCAAATACGGTGAGGATAAAT  
 CTCTAAACAGATTGCGCGTAAGATTGAGCAAGCGCGTGAAGTGAAGCCGATTGAGACAAGGACTGAGTT  
 AGCAGAGATTATCAAGTTGGTCAAACTGCCAAGGAAGTCAAGAAAGAGGGTCACTCTGCTAAGCAGAT  
 TTCCAGGCTATTGCAATTGAAGTCAATGATGAAGTGGGAGCGGCAGATGAGTCCATCCAGCAGGCTATG  
 CATATGTTGGCTCTGGATGGTAGAATTTCAAGTATTACCTTTCAATTCCTTAGAAGACCGCTTGACCAAGCA  
 ATTGTTCAAGGAAGCTTCAACAGTTGAAGTTCCAAAAAGGCTTGCCTTTTCATCCAGATGATCTCAAGCCC  
 AAGATGGAATTTGGTGTCCCGTAAGCCAATCTTGCCAAGTGCGGAAGAGTTAGAAGCCAATAACCGCTCG  
 CACTCAGCCAAGTTGCGCGTGGTCAAGAAAAATTCACAAGCTCGAGCACCACCACCACCACCACTGA

## 2 CFE21 "homologue of SEQ. ID NO. 19"

ATGAGTGAATTTTAGATAATGAGATAATGGGGATGAGGAGTTAGTAGAACCGCAGCTCCGCTCCTCAG  
 TATTTACGTGAATATATCGGACAAGATAAGGTCAAGGACCAGGTACAAATCTTTATGAAGCTGCCAAAA  
 TCGGGATGAAGCGCTGGATCATGTGCTCTTATTTGGGCTCCAGGTCTCGGGAAAAACGACCATGGCCTT  
 TGTATTGCCAACGAAGTGGAGTCAATCTTAAGCAGACGTCGGGTCCAGTCATTGAAAAAGCCGAGAT  
 CTGGTAGCTATTTGAATGAGTTAGAGCCTGGGGATGTCTTTTATTGATGAGATCCATCGTTTCCCAAT  
 GTCAGTGAAGAGGTGCTTTATAGTGCTATGGAGGACTTCTACATAGATATTATGATTGGGGCTGGTGAG  
 GGTAGTGTAGTGTTCATTGAGTTACCACTTTTACCTTGATTGGTGGGACGACTCGGGCTGGTATGCT  
 CTCCAACTCCGTACGGGCACGTTTGGGATTACAGGCCATATGGAGTATTATGCCCATGCTGACTTGACA  
 GAATTTGTCGAGCGGACCGGCAGATATTTTGAATGGAATCACTCATGAGGCAGCATCTGAGTTGGCCC  
 TACGTAATCTGTCGGACCCCTCGTATTGCCAATCGTCTCCTCAAGCGCGTGGCGGATTGTCAGATAATG  
 GGAATGGGGTAATTGATGATATTATACGATAAGGCTTTGACTATGCTGGATGTTGACCATGAAGGTT  
 TGGACTATGTGATCAAAAAATCCTTCGTACCATGATTGAGATGTACAGTGGAGGACCTGTTGGTCTAGG  
 AACTCTTCTGTGAATATCGCGGAAGAGCGTGAGACAGTTGAAGACATGTATGAGCCTTACTTGATTCAA  
 AAGGTTTATCATGCGGACACGGTCTGGACGGGTGGCGACTGCTAAGGCATATGAGCACTTAGGTTATG  
 AATACAGTGAAGAAAGCGGCCGCACTCGAGCAACCACCAACCACCACCACTGA

## 2 CFE24 "homologue of SEQ. ID NO. 20"

ATGAGTATGTTTTTAGATACAGCTAAGATTAAAGTCAAGGCTGGTAATGGTGGCGATGGTATGTTGCCCT  
 TTCCTCGTGAAGAAATATGTCCTAATGGAGGCCCTTGGGGTGGTGATGGTGGTCTGGAGGCAATGTTGT  
 CTTCGTTGTAGACGAAGGACTACGTACCTTGATGGATTTCGGCTACAATCGTCATTTCAAGGCTGATTCTG  
 GTCAAAAAGGGATGACCAAAAGGATGTCATGGTGGTGGTGGTGGTGGTGGTGGTGGTGGTGGTGGTGGT  
 GTACGATGTTTGGTATGCGGAGACTGGCAAGGTTTAAACAGATTGATTGAACATGGGCAAGAAATTTAT  
 CTTTGGCCACGGT  
 ATCTCTGAAAAATGGAGAACCAGGTCAGGAACGTGAGTTACAATTGGAACATAAAAAATCTTGGCAGATGTC  
 GGTTAATAGGATTCCCATCTGTAGGGAAGTCAACACTTTTAAAGTGTATTACCTCAGCTAAGCCTAAAAAT  
 TGGTGGCTACCACTTACCCTATTGTACCAAAATTTAGGATGTTTGGCACCCTAATCAGGTGAATCCTTTG  
 CAGTAGCCGACTTGGCAGGTTTGATTGAAGGGGCTAGTGAAGGTGTTGGTTTGGGAAATCAGTTTCTCCG  
 TCACATGAGCGTACACGTGTTATCCTTCACATCATGATATGTCAGCTAGCGAAGCCCGTGATCCATATG  
 AGGATTACCTAGCTATCAATAAAGAGCTGGAGTCTTACAATCTTCGCTCATGGAGCGTCCACAGATTAT  
 TGTAACTAATAAGATGGACATGCCTGAGAGTCAGGAAAAATCTTGAAGAATTTAAGAAAAAATTTGGCTGA  
 AAATTATGATGAATTTGAAGAGTTACCAGCTATCTTCCCAATTTCTGGATTGACCAAGCAAGGTCTGGCA  
 ACACTTTTAGATGCTACAGCTGAATTGTTAGACAAGACACCAGAAATTTTGTCTTACGACGAGTCCGATA  
 TGGAGAAGAAGTTTACTATGATTTGACGAAGAAGAAAAAGCCTTTGAAATTAAGTCTGATGACGATG  
 CGCATGGGTATTTCTGGTGAAGAACTCATGAACTCTTAAATATGACCAACTTTGATCGTGTATGAATCT  
 GTCATGAATTTGCCGTCAGCTTCTGGGTATGGGGGTGATGAAGCCCTTCTGTCGGGTGGAGCTAAAG  
 ATGGGATTTGGTCCGCAATTGGTAAATTTGAGTTTGAATTTGTAGACCTCGAGCACCACCACCACCACCA

## 2 CFE25 "homologue of SEQ. ID NO. 21"

ATGAAC TACITTAATGTTGGGAAAATCGTTAATACGCAGGGATTACAGGGTGAGATGCGAGTCTTGCTG  
 TGAAGGATTTTGCAGAAGAACGGTTTAAAAAGGAGCTGAGCTGGCTTTGTTTGATGAAAAAGATCAGTT  
 TGTCAAACAGTGACCATCGCTAGCCACCGTAAACAGAAGAACTTTGACATTATTAATTCAAAAGATATG  
 TACCATATCAATACTATCGAAAAGTACAAGGGATACAGTCTCAAGGTCGCTGAGGAAGATTTGAATGAC  
 CTAGACGATGGTGAATTTTACTATCAGGAGATTATCGGTTTGGAAAGTCTATGAGGGTGATAGCTTGCTG  
 GAAACATCAAGGAAATCCTGCAACCAAGGTGCTAATGATGTCTGGGTGGTCAAAACGAAAAGGCAACCGTG  
 ATTTCCTTTTACCTTATATCCACCAAGTGGTCTCAATGTTGATATCCAAATAAACGGGTGATGTGGAA  
 ATCTTAGAAGGCTTAGACGATGAAGATCTCGAGCACCACCACCACCACCTGA

## 2 CFE26 "homologue of SEQ. ID NO. 22"

ATGAAGATTGATATTTTAACCTCTTTCCAGAGATGTTTCTCCACTGGAGCACTCAATCGTTGAAAAGGC  
 TCGAGAAAAAGGGCTCTTGGATATCCAGTATCAATTTTCGAGAAAATGCTGAAAAGGCCCGTCATGTA  
 GATGATGAGCCCTACGGAGGCGGTGAGGGCATGTTGCTCAGAGTACAACCTATTTTGGATTCTTTGATG  
 CTATTGAAAAAGAAAATCCGCGCGTTATTTCTCTCGATCTGCTGGAAGCAGTTTGATCAGGCTTATGC  
 TGAAGATTGGCTCAAGAGGAAGAGCTAATCTTTATCTGTGGGCACTATGAGGGTTATGATGAGCGCATT  
 AAGACCTTGGTAACAGATGAGATTTCCCTAGGCGACTATGTTCTCACTGGTGGAGAATTGGCAGCTATGA  
 CCAATGATTGATGCTACAGTTCCGCTGATTCAGAAAGTATGGCAAGGAGTCTAGCCACCAAGATGATAG  
 TTTTCTTCAGGCTTTTGAATATCTCTCAGTACACAGCTCCCTATGATTATCGAGGCACTGGTCTGCCAG  
 ATGATTTGATGAGTGGTCAACATGAAAAGATTTCGTCACTGGCGATTGTACGAGAGTTTAAAGAAAACCTA  
 CGAGCGCAGGCGGATTACTTGAACATTATCAACTGACAGTAGAAGAAGAAAAATGCTGGCAGAAAT  
 CAAAGAAAAACAAAGAGCGGCGCACTCGAGCACCACCACCACCACCTGA

## 2 CFE27 "homologue of SEQ. ID NO. 23"

ATGATTCGAAGCAAGTAAATTAAGGCTGGTATGACCTTTGAAAACAGCTGACGGCAAATTGATTGCGGTTT  
 TGAAGCTAGTACACACAAACCAGGTAAAGGAAACACGATCATGCGTATGAAATTGCGTGATGTCCGTA  
 CTGGTTTACATTTGACACAAGCTACCGTCCAGAGGAAAAATTTGAACAAGCTATTATCGAGACTGTCCC  
 AGCTCAATACTTGTACAAAAATGGATGACACAGCATACTTCATGAATACAGAACTTATGACCAATACGAA  
 ATCCCTGTAGTCAATGTTGAAAACGAATTGCTTTACATCGTTGAAAACCTGATGTGAAAATCCAATTCTA  
 CGGAATGAAATGATCGGTGTACCGTTCTACTACTGTTGAGTTGACAGTTGCTGAAACTCAACCATCT  
 ATGAAGGTGCTACTGTTACAGGTTCTGTTAAACAGCAACGATGGAACCTGGACTTGTCTAAACGTTT  
 CAGACTTCATGGAAGCAGGAAAAACTCGTTATCAACACTGCAGAAGGAACCTACGTTTCTGTCGCT  
 CGAGCAACCAACCACCACCACCTGA

## 2 CFE28 "homologue of SEQ. ID NO. 24"

ATGCAATTTGAAAATTTAACAGAACGTTTGCAGAACGTTTAAAAATCTACGTAAAAAGGAAAAATCT  
 CTGAATCTGATGTCGAAGAGGCAACCAAGAAATTCGCTTGGCCTTGCTCGAGGCCGACGTTGCCCTTGCC  
 TGTGTAAAGGACTTTATCAAGAAAGTTAGTGAGCGTGAGTGGGCACTGAGGTCATTGATACACTTAAT  
 CCTGCGCAACAGATTATTAATTCGTTGATGAGGAACGACAGCCGTTTATAGGTTCTGATACGGCAGAAA  
 TTATCAAGTCACTAAGATTCCAACCATCATGATGGTTGGTTTACAAGGGGCTGGTAAAAACAACCTT  
 TGGTGGTAAATTGGCCAAACAACTCAAGAAAGAAAGAAATGCTCGTCTTTGATGGTTGCGGCGGATATT  
 TATCGTCCAGCTGCCATTGAACAGCTTAAGACCTTGGGACAACAGATTGATGTGCTGCTTTGCACTTGG  
 AAAGAAAGTACCAAGCTGTTGAGATTGTACGTGAAGTTTGAAGCAAGCCAACTAATCATAAGCACTAT  
 GTCTTGAATGATACTGCGGGTCTGTTGCAAGTTGATGAGCTCCTCATGAATGAGCTTCTGTGATGTGAAAG  
 CATTTGGCTCAACCAAAATGAATCTTGTGCTGCTGTTGATGCTATGATTGGTCAGGAAGCAGCAATGTTGC  
 GCGTGATTTAATGCTCAGTTGGAAGTCACTGGGCTCATCCTTACCAAGATTGATGGCGATACTCGTGGT  
 GGTGCTGCTGCTGCTGTTGCTCATTACTGGAAAACCAATCAAGTTCACTGGTACAGGTGAAAAGATTA  
 CGGACATGAAAACCTTCCACCCAGACCGCATGTCTAGCCGTATCCTTGGTATGGGGGATATGCTCACTT  
 GATTGAGAAAGCTTCTCAGGAATACGATGAACAAAAGCCCTTGAATGGCTGAGAAAGATGCGCGAAAA  
 CACTTTGATTTAATGATTTCTCGATCAATTAGATCAGGTGCAAAATATGGGGCCGATGGAAGACTT  
 CTCAGATGATTCAGGTATGGCCAAACATCCAGCCCTTCAAAACATGAAGGTGGATGAACCCAGATT  
 GCTGTAACCGTGCCATTGTGCTTTCGATGACACCTGAAGAGCGTGAAGAACCAAGATTGTTAAATGCAA  
 GCGTGGCGCTGCTGATTGCTGCTGTTCTGGAATACATTGCTGGAAGTCAATAAATTCATCAAGGACTTT  
 AACAGGCTAAACAGCTCATGCAAGGTGTTATGCTGCGGATATGAATAAATGATGAAGCAAAATGGG  
 ATTAATCAAAATAACCTTCTTAAAAATATGCCAAATATGGGAGGAATGGATATGCTGCGCTTGAAGGAA

## 2 CFE 28 (Contd.)

(Contd.)  
 Fig 49  
 TCATGGGACAAGGCGGTATGCCTGACTTATCAGCTCTCGGAGGAGCAGGAATGCCAGATATGAGCCAGA  
 TGTTCGTGGCGGTTTGAAGGTAATAATTGGTGAATTTGCCATGAAACAGTCCATGAAACGTATGCTAA  
 CAAAATGAAGAAAGCGAAGAAGAAACGCAAGGCGGCCGCACTCGAGCACCACCACCACCACCTGA

## 2 CFE29 "homologue of SEQ. ID NO. 25"

Fig 50  
 ATGTATCTTATTGAAATTTTAAATCTATCTTCTTCGGGATTGTTGAAGGAATFACGGAATGGTTGCCGAT  
 TTCCAATACAGGTCACCTTGATTTTAGCAGAGGAGTTTATCCAATACCAAAATCAAAATGAAGCCTTTATG  
 TCCATGTTAATGTGCTGATTCAGCTTGGTGCTATTTTAGCAGTTATGGTGATTTATTTTAAACAGCTCAAT  
 CCTTTTAAACCGACTAAGGACAAACAGGAAGTTCGTAAGACTTGGAGACTATGGTTGAAGGCTTTGATTG  
 CCACITTCGCTTTACTTGGTGCTTTAAATTTGATGATTGGTTTQATACCCACTTCCATAACATGGTTTCAG  
 TTGCTGTCTATGTTGATTATCTACGGGGTTGCCCTTCATCTATTGGAAAAGCGCAATAAAGCGCGTGCTATC  
 GAGCCAAGTGTAACAGAGTTGQACAAGCTTCCTTATACGACCGCTTCTATATCGGACTCTTCCAAGTTCT  
 TGCTCTTTTACCAGGGACTAGCCGTTCAAGGTGCAACGATTGTCGGTGGTTTGTAAATGGAACCAAGTCGTT  
 CAGTTGTGAGAGAATTTACCTTCTATCTTGGGATTCCCGTTATGTTTGGAGCTAGTGCCTTAAAGATTTTC  
 AAATTGTGAAAGCCGGAGAATCTTQAGCTTTGGGCAATTGTTTTGCTCTTGGTGGGATGGGAGTAG  
 CTTTTCGGTCAGCATGGTGGCTATTGCTTCTTGACCAGCTATGTGAAAAAACACGACTTCACCCCTTTT  
 GGTAAATACGGTATCGTGCTTGTAGTGTTTTGCTACTTTACAGTTTGTCCGTTTATTGTACTCGAGCAC  
 CACCAACCACCACCTGA

## 2 CFE30 "homologue of SEQ. ID NO. 26"

Fig 51  
 ATGGGATTATTTGACCGTCTATTTCGGAAAAAAGAAAGAACTTAAATCGAAGAAAGTTGTAAGAAGAGCT  
 CTGAAAAATCTTGATTGTCTGAAGATGTTGATCCTACCTTCACAGAAAGTTGAGGAAGTTTCTCAGGAAG  
 AAGCAAGAGGTTGAAATTTGTAACAAGCTGTGTTCCAAGAAGAGGAAATCCAAGACACAGTTGAAAGAAA  
 GTCTGGATTTAGAGCCAGTTGTAGAAGTTTCTCAAAAAGAAAGTGAAGAATTTCCCACTCAGAAGAAGG  
 GAATAGTGAGTTTCTAGAGACTATAGAAGAAAATAATTCTGAAGTTCTTGAACCAGAAAGGCCCTCAAGC  
 AGAAGAAACCGTTCAGGAAAAATATGACCGCAGTCTTAAAGAAAACCTGACAGGTTTCGGTGGCCGCTT  
 CAATGCTTCTTCTTAACTTCCGCTCTGTTGACGAAGAATTTTTCGAGGAAGTGAAGAAGCTGCTGATTA  
 TGAGTGATGTTGGTGTCCAAGTCGCTTCTAACTTAAACGGAAGAACTACGTTACGAAGCCAAAGCTTGA  
 TGCCAAAGAAACCTGATGCACTTCGTCGTGTCATCATTTGAGAAAATGTTGAGCTTTATGAAAAGGATGGT  
 AGCTACGATGAAAGCATCCACTTCCAAGATAAATGACAGTTATGCTCTTTGTTGGTGTGAATGGTGTG  
 GGAAAAACAATCTTATCGGAAAACTAGCCACCGCTACAAACAAGCTGGTAAGAAGGTCATGCTGTTG  
 CAGCAGATACCTTCCGTGCGGGTGCAGTAGCTCAGCTAGCTGAATGGGGCCGACGAGTAGATGTTCCAGT  
 AGTAACCTGGACCTGAAAAAAGCTGATCCAGCCAGCGTGGTCTTTGATGGTATGGAACGTGCCGTGGCTGAA  
 GGTATCAGATTTCTCATGATTGATACTGCTGGTCTGTGCAAAATAAGGATAACCTTATGGCTGAGTTGG  
 AAAAGATTGGTGGTATTATCAAAACGTTGTGTCAGAAAGCAACCATGAACCTTCTGGCACTTGAATGCA  
 TCAACAGGTCAAAATGCCCTAGTACAGGCCAAAGAAATTTTCGAAAAATCACACCTTTAACGGGAATTTGTT  
 TGAATAAGATTGATGGAAGCTGCTCGAGGAGGTGTGGTTCTAGCCATTGCTGAAGAAGCAATATTCTGT  
 AAAATTGATTGGTTTGGTGAAAAAATCGATGATATTGAGAGATTTAACTCAGAAAACTTTATGAAAGGT  
 CTGTTGCAAGGTTTAAATCGCGCCGCACTCGAGCACCACCACCACCACCTGA

## 2 CFE31 "homologue of SEQ. ID NO. 27"

Fig 52  
 ATGTATATTGAAATGGTAGATGAAAGTGTCAAGTTTCAAAAGAAATGTTGCAACAAACCCAAGAAATTT  
 TGAATTTGCAGCCCAAAATTAAGAAAGAAAGACAAGGAGATGGCAGTCACTTTTGTGACCAATGAGC  
 GTAGTCAATGAATTAATCTGGAGTACCGTGACACCGACCGTCCGACAGATGTCATCAGCCTTGAGTATAA  
 ACCAGATTGGAAATGGCTTTGACCAAGAGGATTTGCTTGAATTCAGAAATGGCAGAGATGATGTCT  
 GACTTTGATGCTATATTGGGGAATTGTTCACTCTATCGATAAGGCTCATGAGCAGGCCGAAGAATATG  
 GTACAGCTTTAGCGTGAAGATGGGCTTCTTGGCAGTACACGGCTTTTACATATTAACGGCTATGATCAC  
 TATACTCGGAAGAAAGCGGAGATGTTGGTTTACAAGAAGAAATTTGACAGCCTATGGACTCACA  
 AGCAACTCGAGCACCACCACCACCACCTGA

## 2 CFE32 "homologue of SEQ. ID NO. 28"

Fig 53  
 ATGAGTATTCGAGTAATTTATGCGGTTTAAAGGGAAAGATGGGCCAGGCTGCTTGTGAGATGGTATTGA  
 CTGATCCAGACTTGAATTTGGTGGCAGTTTGGATCCTTTTGAATCTGAGTCAGAAATGGCAAGGATTTCT  
 GTTTTCAAGGATAAGGCTGATTAGCTGGTTTGAAGCGGATGCTGGGTAGATTTTACTACTCCAGCTGT  
 TGCTAGCAAAATACAGTTTGTCTTGAATAAGGCTTGTCTCCAGTAGTTGGAACGAGTGGTTTCACGA

2CFE32

Fig 53 (contd.)

GTGAAGAAATTGCAGAGCTAAAAGAATTTCTCGTGCCCAAGACTTGGGTGGCCTGATTGCCCTAACTT  
 TCCCTTGGGTGCTGTCTTACTCATGCAATTTGCGACGCAGGCTGCCAAATAATTCCCAAATGTGGAGATTA  
 TTGAGCTCCATCATGACAAGAAAAGGATGCTCCGAGTGGAACAGCCATTAAACAGCTGAAGTTGATGG  
 CAQAGGTTTGAAGTCCATTGACCAAGGCGCAGCAGATGAGGAAGAGCTGATTGCTGGTGTCTGGTGGT  
 CTGACTTTGATGGTATGCGCATCCACTCAGTTTCGTTTGCCAGGCTTGGTAGCTCATCAAGAAGTCATCTTT  
 GCGCAATCAGGGAGAAGGGTTGACCTCCGTCATGACTCCTATGATCGCATCTCCTTCATGACAGGAGTCA  
 ATTGGGAATTAAAGAAGTTGTCAAGCGTCATGAGCTTGTCTATGGATTAGAACACTTATTACTCGAGCA  
 CCACCACCACCACCTGA

Fig 54

2CFE33 "homologue of SEQ. ID. NO. 29"

ATGGCAACAAACAAGATTTGATCGCTAAAGTAGCAGAAGCTACAGAATTGACTAAGAAAGACTCAGCA  
 GCAGCATTTGAAGCTGTATTTGCAAGCAGTAGCTGACTATCTTGCAGCTGGTGAAAAAGTTCAATTGATCG  
 GTTTTGGTAACTTTGAAGTTGCTGAGCGTGCAAGACGTAAAGGTCGCAACCCACAACTGGTAAAGAAAT  
 GACAAATTCAGCTTCTAAAGTACCAGCATTCAAAGCTGGTAAAGCTCTTAAAGACGCTGTAAACTCOAG  
 CACCACCACCACCACCTGA

Fig 55

2CFE34 "homologue of SEQ. ID. NO. 30"

ATGACTAAAAAGCCTTTTATTGCTGGTCAAGGTGCCAGTATCTAGGGATGGGACGGGATTTCTATG  
 ATCAOTATCCGATTGTTAAAGAAACGATTGATCGAGCGAGTCAGGTGCTAGGTTATGATTTGCGTTATGT  
 CATCGATACGGAAGAAGACAACTCAATCAGACCCGCTATACGCAACCAAGCCATTCTAGCGACTTCGCTT  
 CCTATCTACCGTTTATTGCAAGAAAAGGGCTATCAGCCTGATATGGTTGCTGGTTTGTCTCTGGAGAAAT  
 CTCTGCTTGTGCGCAAGCGCGCCTTGGATTTTGAAGATGCGGTTGCTTGGTAGCTAAGCGTGGAGCC  
 TATATGGAAGAAGCGGCTCCTGCTGACTCTGGCAAGATGGTAGCAGTTCTCAATACGCCAGTAGAGGTGA  
 TTGAAGAAGCCTGTCAAAAAGCTTCTGAACTTGGAGTGGTTACTCCAGCCAATATAACACACCTGCGACA  
 AATCGTCATTGCTGGAGAAAGTGGTTGCAGTTGATCGAGCGGTGAACCTTTGCAAGAAGCAGGTGCCAAA  
 CGCTTGATTCTCTTAAGGTGTCAGGTCCCTTTACACCTCTCTCCTTGAACCTGCTAGCCAGAAACTAGC  
 TGAACCTCTGCTCAGGTAAGTTTTCAGATTTTACTTGTCCCTAGTCGGCAATACAGAAGCTGCTGTGA  
 TGCAAAAAGAGGACATTGCTCAGCTCTTGACGCGTCAGGTCAAGGAACCCGTTGCTTTCTATGAAAGTAT  
 TGGGCTCATGGAAGAAGCAGGCATAAGCAACTTATCGAGATTGGAACCGGGAAAGTCTTGTGAGGTTT  
 GTTAAAAAATTTGATCAAACTGCTCACTTAGCTCATGTGGAAGATCAAGCGAGTTTAGTAGCACTTTTAG  
 AAAAACTCGAGCACCACCACCACCACCTGA

Fig 56

2CFE35 "homologue of SEQ. ID. NO. 31" 35

ATGAACTAGAACATAAAAAATATCTTTATTACAGGTTCCGAGTCGTGGAAATGGTCTTCCATCGCCCA  
 AGTTTGTCAAGCAGGAGCCAACATTGTCTTAAACAGTCGTGGGGCAATCTCAGAAGAATTGCTGCTCA  
 GTTTTCAAACTATGGTATCAAGGTGGTTCCCAATTCAGGAGATGATCAGATTTTGCAGACGCTAAGCGT  
 ATGATTTATCAAGCTATTGCAAGACTGGGTTCAAGTAGATGTTTGGTCAAGAAATGCAAGGATACCAAG  
 ATACTCTTATGCTCAAGATGACAGAAGCAGATTTGAAAAAGTGCTCAAGGTCATTTGACTGGTGCCTT  
 TATATGACAGAATCAGTCTTGAACCGATGATGAAAGCGAGAGAAAGGTGCTATCATTAATATGCTACT  
 GTTGTGGTTTGTATGGGGAAATATTGGTCAAGCTAACTATGCTGCTTCAAGGCTGGCTTGAATTGGCTTAC  
 CAAGTCTGTGGCAGCGAGGTCGCTAGTCCGAATATACGAGTCAATGTGATTGCTCCAGGAATGATTGAG  
 TCTGATATGACAGCTATCTTATCAGATAAGATTAAAGGAAGCTACACTAGCTCAGATTCCGATGAAAGAAT  
 TTGGGCAGGCAGAGCAGGTTGCAGATTGACAGTATTTTAGCAGGGCAAGATTATCTAATGCTCAAGT  
 GATTGCCATTGATGGTGGCTTAAGTATGCTCGAGCACCACCACCACCACCTGA

Fig 57

2CFE36 "homologue of SEQ. ID. NO. 32"

ATGGGAGTGAAAAAGAACTAAAGTTGACTAGTTTGCTAGGACTGTCTCTGTTAATCATGACAGCCTGTG  
 CGACTAATGGGTTAACTAGCGATATTACAGCCGAATCGGCTGATTTTGGAGTAAATGGTTTACTTCTTT  
 GCGGAAATCATTCGCTTTTATCGTTTGAATTAGTATCGGAGTGGGGATTATCTCTTTACGGTCTTGAAT  
 COTACAGTCTCTTGGCAGTCTTTCAGGTGCAAAATGGTGGCTTCTAGGAAAAATGCAGGAAGCTCAGCCAC  
 GCATTAAAGGCTTTCGAGAACAATATCCAGGTGCAATATGGAAGCAAGCAACCAACTAGAGCAGGAAA  
 TGGCTAAAGTATTTAAAGAAAATGGGTGTCAGACAGTCAGACTCTCTTTGGCCGATTTTGATTGATGCG  
 GGTATTTTGGCCCTGTTCAGCCCTATCAAGAGTTGACTTTTAAAGACAGGTCAATTTCTTATGGATTA  
 ACCTTGGTACTGTGGATACAACCTTGTCTTCCGATTTTAGCAGCAGTATTCACCTTTTAAAGTACTTGG  
 TTGTCCAACAAAGCTTTGTCTGAGCGAAATGGCGCTACGACTGCGATGATGATGGGATTCCAGTCTTGA  
 TTTTATCTTTGAGTTTATGCGCCAGGTGGAGTCGCCCTATACTGGACAGTGTCTAATGCTTATCAAGTC

(Cont'd)  
Fig 57

2 CFE 36

TTGCAAACTATTCTTGAATAATCCATTCAAGATTATCGCAGAGCGCGAGGCCGTAGTACAGGCACAAA  
AAGATTGGAAAAATAGAAAAAGAAAAGCCAGAAAAAGGCTCAGAAAAACGAACTCGAGCACCACCAC  
CACCACCACTGA

2 CFE37 "homologue of SEQ. ID NO. 33"

ATGAAGATTAGTAAGAGGCACCTATTAAATTATTCCATTCTTGATTCCCTACTTGCTTTTATCTATTTTGGGC  
TTGATTGTGGTCTATTTCGACCACCAAGTGCTATTTAATTGAAGAAGGCAAGAGCGCCTTGCAAGTTGGTTCC  
AAACCAAGGAATCTTTTGGATTGGTAGTTTGATACTGATTGCTTAATTTATAAATTGAGACTAGATTTT  
TGAGAAATGAGCGACTAATCAATTTAGTTATATTAATAGAAATGCTTTTATTGTTCTTGCTCGTTTATT  
GOTATTTCAGTAAACCGGGCATAACGGTTGGATTTCGGTTGCAGGAGTAACTATTCAGCCAGCTGAGTACT  
TAAAAATCAATTATTATTGGTATTAGCTACCGATTCTCAAACAGCAAGAAGAAATAGCTACTTATGA  
TTTTCAAGTTTITGACTCAAAATCAATGGCTTCCCGTGCTTTAATGATTGGCGATTGCTTCTCCTAGTTCT  
GATTGGAAGTTTGGGAATTTCCCTGATTTAGGAAATGCGACTATTTTAGTCTTGTTTCTGTTGATTATGT  
ATACAGTTAGTGGAAATCGCTTATCGCTGGTTTCAACCAATTCTGGCGCTCGTATCTGCGCGTTCTGCTTTG  
TCTTGAACCACTATCAGCCTAATCGGTGTTTGAGACCTTTTCAAAAATTCAGTATTTGGCTATGTAGCCAAA  
CGCTTATAGTGCCTTTTAAATCTTTTGGCGATCGTCTGATGCAGGTCAACAGTTAGCTAATCTTATTTT  
GCCATGTCAATGGTGGTTGGTTTGGTCTAGGTCTTGGAACTCGATTGAAAAACGAGGTTATTTGCCAG  
AAGCTCATAACAGACTTTGTCTTTTCTATCGTATTGAAAGAAATTTGGCTTTGTTGGTGCCAGTCTTATTTAG  
CTCTCTTGTTTTTCATGATTTTGGCGATTATCTTGGTGGTATTTCGAGCGGAGAAATCCTTCAATGCCATGG  
TTCACTCGGTGTCGGAGGGAATGATGTTGGTTCAAGTATTTGTCAATATCGGAGGGATTTCGGGCTTGATT  
CGATCTACAGGAGTAACCTTCCCTTCTTATCCAGGGTGAAATAGTCTTCTAGTCTTATCAGTGGCACT  
ACCTTCTCTTAAATATTGATGCCAGTGA AAAACGCGCTAAGTTGTACCGAGAATTGGA AAAATCAACCA  
ATGAACCTTCTGTTGAAGCTCGAGCACCACCACCACCACCACTGA

Fig 58

2 CFE38 "homologue of SEQ. ID NO. 34"

ATGCTCGGAATTTTAACTTTATTCTGGTTTTCGGGAATTATGATGTTGTCACGAGTTCCGGGCACTTCTA  
CTTTGCCAAGAAATCAGGGATTTAGTACGTGAATTTGCCATCGGTATGGGACCTAAAAATTTTGCTCACA  
TTGCCAAGGATGGAACGGCCTATACCATCGAATCTTGCTCTGGGTGGCTATGTCCGCATGGCGGTTG  
GGTATGATACAACTGAAATCAAGACAGGAACGCCGTGTAGTTTGACACTTGCTGATGATGGTAAAGGTT  
AAAGGATCAATCTCTCAGGTAAAAAATGGATCAAAACAGCCCTCCCTATGCAGGTGACTCAGTTTGATT  
TTGAAGACAAGCTCTTTATCAAAAGGATTGGTTCTGGAAAGAAAGAAAAACATTTGCAGTGGATCAGGATGC  
AACGGTTGTGGAAGCAGATGGTACTGAGGTTCCGATTGCACCTTTAGATGTTCAATATCAAAAATGCGACT  
ATCTGGGGCAAACTGATTACCAATTTTGCAGGTCTATGAACAATTTTATCTTAGGTGCTGTTGTTTGTG  
GGTTTAACTTTATGCAGGGTGGTGTGAGAGATGTTGATACCAATCAGTTCCATATCATGCCCAAGGTTG  
CCTTGGCCAAAGGTAGGATACCAAGAAACGGCAAAATACCAAGATTGGCTCACAAGGTTAGCAACT  
GGCAAGGCTTGATCCAAAGCTGTGGAAACAGAAACCAAGATAAGACGGCAACCGACTTTGGATGTGACTA  
TTTCTGAAAAAGGGGAGTGACAAAACAGTCACGTGTACACCCGAAGATAGTCAAGGTCCTTACCTTCTAGG  
TGTTCACCGGGGTTAAGTCAGATTTTCTATCCATGTTTGTAGGTGGTTTACAACCTGCTGCTGACTCAO  
CTCTCCCAATCTCTCAGCTCTGAAAAATCTGATTTCCAACCGGATTGAAACAAGTTGGGTGGACCTGTT  
GCTATCTTTAAGGCAAGTAGTGATGCTGCTAAAAATGGAATTGAGAATATCTTGTACTCTTGGCAATGA  
TTTCCATCAATATTGGGATTTTAACTTTATCCGATTCCAGCCTTGGATGGTGGTAAOATTGTGCTCAAT  
ATCTAGAAAGCCATCCGCCGCAACCAATGAAAAAGAAATGAAACCTATGTACCTTGGCCGAGTG  
GTATCATGGTTGTCTTGATGATTGCTGTGACTTGAATGACATTATGCGACTCTTTTAAOACTCGAGCA  
CCACCAACCAACCACTGA

Fig 59

2 CFE39 "homologue of SEQ. ID NO. 35"

ATCTACCATATTTAAAAAGGAATCATTACCAAAATTACTGCCAAATACATTGTTCTTGAAACCAATGGTA  
TTGGTTATATCTGTGATGTGGCAATCCTTATGCCTATTACAGGTCAAGTTAATCAGGAGGCTCAGATTTAT  
GTGATCAGGTTGTGCGTGAGGACGCCATTTGCTTTATGGATTTCGCTCAGAGGATGAGAAAAAGCTCT  
TTCTAGTCTAATTTCCGTTCTCTGGGATTGGTCTGTATCAGCTCTTGTCTATTATCGTCTGATGACAATO  
CTGGCTTGGTTCAAGCCATTGAAACCAAGAACATTACCTACTTGACCAAGTTCCCTAAAAATGGCAAGAA  
AACAGCCAGCAAGATGTTGCTGGAATTGGAAGGCAAGGTAGTAGTTGCAGGAGATGGCTTCTGCCAA  
GGTCCGAGTGCAAGCAAGTGCTGAAAAACCAAGAAATTTGAAAGGAAGCTATGGAAGCCATGTTGGCTCTGGG  
CTACAAAGCAACAGAGCTCAAGAAAAATCAAGAAATTTTGAAGGAACGACAGATACAGCTGAGAACTA  
TATCAAGTGGGCCCTTAAAAATGTTGGTCAAACTCGAGCACCACCACCACCACCACTGA

Fig 60

## 2 CFE40 "homologue of SEQ. ID NO. 36"

ATGAAAGAAATAATCGTATTTTACGACTTCTGGAAATGATATTTTATAGTGGTGGTGGACTGTCAGCTGATTT  
 GGCTACCTATACCTTGAACGGCTTGCATGGGTTTGTAGCAGTGACTTGTGACAGCCTTGACAGAAAAA  
 GGATTGAAGTCTTTCCAAGTATGATACCATTTTCAACATGAATTAGATAGCTTGCCTGATGTGGAATT  
 TGGGGGAATTAAGATTGGTCTTCTCCCTACTGTCAGTGTGGCTGAGAAGGCCTTGGACTTTATCAAAACA  
 CCCCCGGAATACCTGTGGTGTGGATCCTGTCTTGGTCTGCAAGGAAACCGATGATGTAGCTGTCACTG  
 AGCTCTGCCAAGAGTTGATTGCTTTTCCCTTATGTCAGTGTGATTACGCTAATCTCCAGAAAGCAGAA  
 TTATTATCCGTCAGGAAATTAACCTTGGAGACATGAAACTGCAAGCAGAAATTGCATGATTTAG  
 GAGCCGCAAGTCAATTATCAAGGGAGGCAATCGTCTTAGTCAGGACAAGGCTGTGGATGTCTTTTATGA  
 TGGACAGACCTTTACTATCCTAGAAAATCCAGTTATCCAAGGCCAAAATGCTGGTGCAGGTTGACCTTT  
 GCTCTAGCAATGCCAGTCACTTGATTAAAGGTGATAAACTTTTGCCAGCAGTAGAAAGCTTAAGGCTT  
 TCGTTTATCGTGTATTGACACAAGCAGATCAGTATGGAGTAAGACAATATGAAGCAAAACAAAACAACC  
 TCGAGCAACCAACCACCACCCTGA

Fig 61

## 2 CFE41 "homologue of SEQ. ID NO. 37"

ATGATTGAAACGGAGAAAAAGAGGAGCGAGTCTGTGATTGGTGTGGAATTGCAGGGTATGGACAGT  
 TTGACCTCTGCATGGAAGAAATTGGCTAGTTTAGCGAAAACGGCAGGGGAGTCTGTGATAGATAGCTACA  
 GACAAAACCTGAAAAATATGATTCCAAGACCTTCTGCGGCTCTGGTAAAGTTGGAAGAGATTGCGCTTAT  
 GGTGGATGCCAGAAAGAAATCACTAGTGCATCGTCAACCAACCGTCTGACCCCAAGGCAGAAATGTCAATCTA  
 GAGGAAGTTCTCGGTGTTAAGGTCAATTGACCGTATGCAAGTTGATTGATATCTTTGCCATGCGGGCTCG  
 AAGCCATGAAAGGAAGCTCCAAGTCCACCTAGCCCAACTCAAATACCTCTTGGCTCGCTGGTGGTCAAG  
 GGAATATGCTCAGCCGTCAGGCAGGGGGAATGCTTCCCGTGGTCTGTTGAAAGCCAACTGGAGCTG  
 AACCTGCTAGCCTTCGCAATCAAATCACGGATATCGAGCGCCAGCTTAAGGTGTTGAGAAAAATCGT  
 GCGACTGTCAAGAAAAACGTTTGGAGTCTAGCACTTTAAGATTGGTTGATTGGTTATCTAATGCTG  
 GAAAAATCACTATCATGAACATCTTGACCAAGTAAGACCCAGTATGAAGCAGATGAGCTCTTTGCCACTCT  
 GGATGGGACAAACCAAGAGTATTCATCTGGGAGGCAACCTCCAAGTAACCTTGACAGATACCGTTGGCTTT  
 ATCCAAGATTGCGGACAGAGTTGGTGTCCAGTTTCAAGTCAACCTTGGAAAGAAAGCAAGCATGTGGAGCT  
 TTCTGGTTCATGTTATCGATGCTAGCAATCCTTACCACGAGGAGCATGAAAAACGGTCTCTCCATCATG  
 AAAGAAGCTGGACATGGAAGATATCTCTCACTTGACGCTTATAATAAAGCGGATTTGGTGGAGGATTTC  
 CCGCTACCAAACGCCATATACCTCATTTCTGCAAGTGTGAGGACAGTCTGAAAACTTGAAGCATT  
 ATTGCTAGATAAGATTAAGGAAATTTTGAAGCATTACCTTGGCAGTGGCTTTTCAAAGTCTTACAAG  
 ATTCAATGATTAGAGAGTGTGCAATTTCTGGAAGAACGTGATTATCAGGAAGACGGCGAAGTATACAG  
 GCTACATTTCCGAGAAAAATAAATGGAGGTTAGAAGAAATTTATGACCTCGAGCACCACCACCACCA  
 CTGA

Fig 62

## 2 CFE42 "homologue of SEQ. ID NO. 38"

ATGGCAAAAAACATATCCTATGACCCTTGAGGAAAAAGGAGAACTTGAAAAAGATTAGAAAGAAATG  
 AAATTGCTTGGTCCAGCAGAAAGTGGTAGAACGCATTAAGATTGCCCGTTACATCGGTGATCTTTCAAGAA  
 ACAGTGAAGTAAGCAGCTAAGGATGAACAAGCCTTTGTGGAAGGACAAATCTTAGCTTAGAAACAA  
 AAACTCCGCTATGCTGAAATCGTCAATAGCGACGCAAGTGGCCAGGACGAAATAGCGATTGOTAAAAACA  
 TCAACCATCCAAAGAAATTGGTGAGGACGAAAGAAAGTTTATATTATCGTAGGTTCACTGGTGGGATGC  
 CTTTGCAGGTAAGGTTTCAAATGAAAGCCCAATTGGGCAGGCCTTGATTGGCAAGAAAAACAGGTGACAC  
 AGCAACCATTAACCGCCTGTTGGTAGCTATGATGTAAAAATCTTGAAGGTTGAAAAAACAGCCCTCGA  
 GCACCACCACCACCCTGA

Fig 63

## 2 CFE43 "homologue of SEQ. ID NO. 39"

ATGACCAAAATTAATGTAGGCTTGGGAAATCCAGGGGATAAATATTTTGAACAAAAACACAATGTTGGTT  
 TTAGTTGATTGATCAACTAGCGAAGAAACAGAAATGTCATTTTACACACGATAAGATATTTCAAGCTGA  
 CCTAGCACTCTTTTCTAAATGGAGAAAAATTTATCTGGTTAAACCAACGACCTTTATGAATGAAAGT  
 GGAAGAGCAGTTCATGCTTTATTAAGTTACTATGGTTTGGATATGACCAATTTACTTATCATTTACGATGA  
 TCTTGACATGGAAGTTGGGAAATTCGTTAAGAGCAAAAGGCTCAGCAGGTGGTCAATGGTATCAA  
 GTCTATTATTCAACATATAGGAACTCAGGTCTTTAACCGTGTAAAGATTGGAATTGGAAGACCTAAAAAT  
 GGTATGTCAGTTGTTTCATGTTTGTAGTAAGTTGACAGGGATGATTATATCGGTATTTTACAGTCTAT  
 TGACAAAGTTGACCATCTGTAACTAGTATTTACAAGAGAAAAATTTGAGAAAAACAATGCAGAGGTA  
 TAACCGACTCGAGCACCACCACCACCCTGA

Fig 64



## 2 CFE44 "homologue of SEQ. ID NO. 40"

ATGATTTTAAATTACAGGGGCAAATGGCCAATTAGGAACGGAACCTTCGCTATTTATTGGATGAACGTAATG  
 AAGAATACGTGGCAGTAGATGTGGCTGAGATGGACATTACCGATGCAGAAATGGTTGAGAAAGTTTTTG  
 AAGAGGTGAACCGACTTTAGTCTACCACTGTGCAGCCTACACCGCTGTTGATGCAGCAGAGGATGAAG  
 GAAAAGAGTTGGACTTCGCCATCAATGTGACGGGGACAAAAATGTGCAAAAGCATCTGAAAAGCATG  
 GTGCAACTCTAGTTTATATTTCTACGGACTATGTCTTTGACGGTAAGAAACCAGTTGGACAAGAGTGGGA  
 AGTTGATGACCGACCCAGATCCACAGACAGAATATGGACGCACTAAGCGTATGGGGGAAGAGTTAGTTGA  
 GAAGCATGTGTCTAAATTTCTATATTATCCGTAAGCTTGAACAGTTGTAAATGACCAGTACGGTCGTCGAC  
 TTGGAATCGTACCTTGGCTGAGTTTCATGACCTACCTAGCTGAAAATCGTAAGGAATTTGGTTATTAATCATT  
 TGTGAATGATGGCAGAGAAGACACAACATGOTATGATTTTGCAGTTGAAATTTTGAAGATACAGATGT  
 CGAAGTCAAGCCAGTAGATTCCAGTCAATTTCCAGCCAAAGCTAAACGTCCTGCTAAACTCAACGATGAGC  
 CTGGCCAAAAGCCAAAGCTACTGGATTTGTTATTTCCAACTTGGCAAGATGCATTGCAAGAATTTTACAAAC  
 AAGAAATGAGACTCGAGCACCACCACCACCACCTGA

## 2 CFE45 "homologue of SEQ. ID NO. 41"

ATGAAACGTCTCTCGACTCTAGAGTCGATTATAGTTTGGCTCTTGCCAGTATTTTTCTACTGGTCATCGGT  
 CTGGTGGCTATCTATATAGCCGTTAGTCAATGATTATCCCAATAATATCTGCCCATTTAGGGCAGCAGGT  
 CGCGTGGATTGCGCTTGGGGCTTGTGATTGGTTTTGTGGTCTATGCTCTTAAATACAGAAATTTCTTTGGAAGG  
 TGACCCCTTTCTATATATTTAGGCTTGGGACTTATGATCTTGCCGATTGTTATTTATAATCCAAAGCTTAG  
 TTGCATCAACGGGTGCCAAAACTGGGTATCAATAAATGGAATTACCTATTTCAACCGTCAGAATTTAT  
 GAAGATATCCTATATCCTCATGTTGGCTCGTGTCAATTGTCCAATTTACAAAGAAACATAAGGAATGGAGA  
 CGCACGGTTCCGCTGGACTTTTGTAAATTTCTGGATGATCTCTTACCATTCCAGTCTAGTTCTTTTA  
 GCACTTCAAAGTGAAGTGGGACGGCTTTGGTTTTGTAGCCATTTTCTCAGGAATCGTTTTATTATCAGG  
 GGTTTTGGAAATTTATATCCAGTATTTGTGACTGCTGTAACAGGAGTTGCTGGTTCTTAGCTATCT  
 TTAATGCAAGGACGGACGAGCTTTTCTTACCAGATTGGAATGCCGACCTACCAATCAATCGGATTTT  
 GGCTTGGCTCAATCCCTTTGAGTTTGGCCAAACAACGAGTTACCAGCAGGCTCAAGGGCAGATTGCCATT  
 GGGAGTGGTGGCTTATTTTGTGAGGGATTTAATGCTTCGAATCTGCTTATCCAGTTCGAGAGTCAATAT  
 GATTTTACGGTTATTGACAGAGATTTTGGCTTATTTGGCTCTGTCTGGTTATTGCCCTCTATCTCATGTT  
 GATTTACCGTATGTTGAAGATTACTCTTAAATCAAATAACCAGTTCTACACTTATATTTCCACAGGTTTGA  
 TTAGATGTTGCTCTTCCACATCTTTGAGAATATCGGTGCTGTGACTGGACTACTTCTTTGACGGGGATT  
 CCGTTGGCTTTTCAATTCGCAAGGGGATCAGCTATTATCAAGTAATCTGATTGGTGTGGTTTGGCTTTATCG  
 ATGATTTACCAAGCTAATCTAGCTGAAGAAAGACGGGAAAAGTCCCATTCAAACGGAAAAAGGTTGTA  
 TTAACCAAAATTAACCTCGAGCACCACCACCACCACCTGA

## 2 CFE46 "homologue of SEQ. ID NO. 42"

ATGGGAAAAATCATCGGAATCACTGGGGGAATTGCCCTCAGGTAAGTCAACTGTGACAAATTTTCTAAGAC  
 AGCAAGGCTTCAAGCAGTGGATGCCGACGAGCTGCTCCACCAACTACAGAAACCTGGTGGTCTGTT  
 TGAAGGCTAGTACAGCACTTTGGGCAAGAAATCAATCTTGAAGAAACGGAGAACTCAATCGCCCTCTCTA  
 GCTAGTCTCATCTTTTCAAATCCTGAAGAGCAAAAAATGGTCTAATCAAATTCAGGGGGAGATTATCCGTG  
 AGGAATCGCTACTTTGAGAGAACAGTTGGCTCAGACAGAAGAGATTTTCTCATGGATATTCCTTACT  
 TTTTGAAGCAGGACTACAGCGATTGGTTTGGCTGAGACTTGGTTGGTCTATGTGGACCGAGATGCCCAAGTA  
 GAACGCTTAATGAAAAGGGACAGTTGTCCAAAGATGAAGCTGAGTCTCGTCTGGCAGCCAGTGGCCTT  
 TACAAAAAAGAAAGATTGGCCAGCCAGGTTCTTGATAATAATGGCAATCAGAACCCAGGTTCTTAATC  
 AACTGCATATCTTCTTGAGGQAGGTAGGCAAGATGACAGAGATCTCGAGCACCACCACCACCACCT  
 GA

## 2 CFE47 "homologue of SEQ. ID NO. 43"

ATGAGAAAAATTTATTCAATGGTGGATTACCACTGCAAGGTGAAATCACTATTAGTGGTGCTAAAAATA  
 GTGTCGTTGCCCTAATTCAGCTATTATCTTGGCTGATGATGTGGTGACTTTGGATTGCGTTCCAGATATTT  
 CGGATGTAGCGAGTCTTGTGCGAAATCATGGAATTGATGGGAGCTACTGTTAAGCGTTATGACGATGATTT  
 GGAGATTGACCAAGAGGTGTTCAAAATATTCCAATGCCTTATGGTAAATTAACAGTCTTCGTGCATCT  
 TACTATTTTATGGGAGCCTCTTAGGCGGTTTTGGTGAAGCGACAGTTGGTCTACCGGGAGGATGTGATCT  
 TGGTCTCGTGGGATTGACTTACACCTTAAGGCGTTGAAGCTATGGGTGCCACTGCTAGCTACGAGGGA  
 GATAACATGAAGTTATCTGCTAAAGATACAGGACTTCATGGTGCAAGTATTTACATGGATACGGTTAGTG  
 TGGGAGCAACGATTAATACGATGATTGCTGCGGTTAAAGCAAATGGTCTACTATTATTGAAAAATGCAGC

## 2 CFE 47 (Contd.)

Fig 68 (Contd.)

CCGTGAACCTGAGATTATTGATGTAGCTACTCTCTTGAATAATATGGGTGCCCATATCCGTGGGGCAGGA  
 ACTAATATCATCATTATTGATGGTGTGAAAGATTACATGGGACACGTCATCAGGTGATCCAGACCGCA  
 TTGAAGCTGGAACATATATCTTTAGCTGCTGCAGTTGGTAAAGGAATTCGTATAAATAATGTTCTTTAC  
 GAACAACCTGGAAGGGTTTGTGCTAAGTTGGAAGAAATGGGAGTGAGAATGACTGTATCTGAAGACAGC  
 ATTTTGTCTGAGGAACAGTCTAATTTGAAAGCAATCAATATTAAGACAGCTCCTTACCCAGGCTTTGCAA  
 CTGATTTGCAACAACCGCTTACCCCTCTTTTACTAAGAGCGAATGTCGTGTGACAATTGTGATACGATT  
 TACGAAAAACGTGTAATCATGTTTTTGAAC TAGCAAAGATGGATGCGGATATTTGACAACAAATGGTC  
 ATATTTGTACACGGGTGGACGTGATTACGTGGGCGCAGTGTTAAAGCGACCGACTTAAGAGCTGGGGC  
 TGCAC TAGCTATTGCTGGGCTTATGGCTGAAGGCAAACTGAAATTACCAATATCGAGTTTATCTTACGT  
 GGTATTCTGATATTATCGAAAAATTACGTAATTTAGGAGCGGATATTAGACTTGTGAGGATCTCGAGC  
 ACCACCAACCACTGA

## 2 CFE48 "homologue of SEQ. ID NO. 44"

Fig 69

ATGTCAAGAATTGAATTTTACCACATCTTTGATGACCATGGATTTGACAAAATTCAAAGAGCAGATTACTTT  
 TTGAATGATAAAGTAGCATCTTATCATATCGATATTATGGATGGCCATTTTGTTCCTCAATATTACCTTGT  
 CTCCTTGGTTCTATTCAAGAAAGTTCAAAAAATTAGTGACACACCTTTATCAGTTTCATCTGATGGTCACAGAC  
 CCAACCTTTTGGGTAGATCAAGTTCTCGAATTTACAATGTGAGTATATTTGTATTTCATGCTGAAGTTCTGAA  
 TGGTCTTGGCTTTTCGTTTGATTGATAAAATTCATGATGCAGGTCTAAAGGCTGGTGTGCTCTTAATCCTG  
 AAACAAGCTGTTTCTACAATCTTTCCCTACATTTGATTTACTTGACAAAAGTAACTATTATGACTGTAGATCCA  
 GCTTTTGCAGGACAACCGCTTTTGGAGTCTACCTTGATAAAATCCAAGAACTCCATCAGCTTAGAGTTCA  
 GAATGCTTATCACTACATCATGAGATGGATGGTTCTTCGAGTCGTAAAGACTTTCAAACAAATTTGATGTG  
 GCAGGACAGATATTTATGTTATAGGTGCGAGTGGATTATTGGTTTGGATGACGATATTGGCAAAGCCT  
 GCGATATCTGTTCTAGAGATTACGAAGAAATGACCGGAAAAACAATGCCAATCAAACCTCGAGCACCAACC  
 ACCACCACTGA

## 2 CFE49 "homologue of SEQ. ID NO. 45"

Fig 70

ATGAGAAATA TGGCTTTGACAGCAGGTATCGTTGGTTTGCCAAACGTTGGTAAATCAACACTATTTAATG  
 CAATTACAAAAGCAGGAGCAGAGGCAGCAAACCTACCCATTTGCGACTATTGATCCAAATGTTGGAATGG  
 TGGAAGTTCCAGATGAACCGCTACAAAACTAACTGAAATGATAACTCCTAAAAAGACAGTTCCACAA  
 CATTTGAATTTACAGATATTGCAGGGATTGTAAAAGGAGCTTCAAAAAGGAGAAGGGCTAGGGAATAAAT  
 TCTTGGCCAATATTTCGTGAAGTAGATGCGATTGTTCACTGAGTTCGTGCTTTTGAATGATGAAAAATGTAATG  
 CGGAGCAAGGACGTGAAGACGCTTTGTAGATCCACTTGCAGATATTGATACAATTAATCTGGAATTA  
 TTCTTGGTGACTTAGAATCAGTGAACAAACGATATGCGCGTGTAGAAAAAGATGGCACGTACGCAAAAAAG  
 ATAAAGAAATCAGTAGCAGAATTCAATGTTCTTCAAAAGATTAAACCAGTCTAGAAAGACGGGAAATCAG  
 CTGTAACCATTAATTAACAATGAGGAACAAAAGGTTGTCAAAGGTTCTTTCTTTTGACGACTAAACC  
 AGTTCTTTATGTAGCTAAATGTGGACGAGGATGTGTTTTCAGAACCTGACTATCGACTATGTCAAACAA  
 ATTCTGAATTTGCAGCGACAGAAAAATGCTGAAGTAGTCTGTTATTTCTGCGCGTGTGAGGAAGAAATTT  
 CTGAATTTGATGATGAAGATAAAAAAGAGTTTCTTGAAGCCATTGGTTTGACAGAATCAGGTGTAGATAA  
 GTTGACCGCTGCAGCTTACCACTTGTGATTGGGAACCTTACTTACAGCTGGTGAAGAAAGAAAGTTCCG  
 GCTTGAACCTTCAAACGTGGTATGAAGGCTCCTCAAGCAGCTGGTATTAATCCACTCAGACTTTGAAAAAG  
 GCTTTATTCGTGCAATAACCATGTATGAAGATCTAGTGAAATATGGATCTGAAAAAGGCGGTAAAAAGA  
 AGGTGGACGCTTGGCTGAAGAAGGAAAAAGAAATATCGTTCAAGATGGCGATATCATGGAATTCGCTTT  
 AATGCTCTGAGCACCAACCAACCACTGA

## 2 CFE50 "homologue of SEQ. ID NO. 46"

Fig 71

ATCGAAATCGAAAAAACCAATCGTATGAATGCGCTCTTTGAATTTTATGCGCGCCTTTTGACAGATAAGC  
 AAATGAATTATATCGAGCTCTACTACGCTGATGATTACAGCCTTGCTGAAATTGCCGAGGAGTTCCGGTGT  
 CACTCGTCAGGCTGTCTATGACAATATCAAGCGAACAGAAAAAGATTCTGGAAGATTATGAGATGAAAT  
 GCACATGTACTCGGACTATATTGTCCGCACTCAGATTTTGTATCAGATTTTGGAGCGCTATCCCAAGGATA  
 ACTTCTCTCAGGACGAGATAGAAATTTTAAACAGCATTGATAATAGAGAACTCGAGCACCAACCAACC  
 ACCACTGA

## 2 CFE51 "homologue of SEQ. ID NO. 47"

Fig 72

ATGACCTTAGAATGGGAAGAATTTCTAGATCCTTACATTCAAGCTGTTGGTGAGTTAAAGATTAAACTTC  
 GTGGTATTCGTAAGCAATATCGTAAGCAAAATAAGCATTCTCCAATTGAGTTTGTGACCGGTGAGTCAA  
 GCCAATTGAGAGCATCAAAGAAAAATGGCTCGTCTGGCATTACTTATGCGACCTTGGAAACAGATTG



## 2 CFE 51 (contd)

Fig. 72 (contd)

CAGGATATTGCTGCTTACGTGTGATGGTTTCAGTTTGTAGATGACGTCAAGGAAGTAGTGGATATTTTGC  
 ACAAAGCGTCAGGATATGCGAATCATACAGGAGCGAGATTACATTACTCATAGAAAAGCATCAGGCTATC  
 GTTCCATCATGTGGTAGTAGAATATACGGTTGATACCATCAATGGAGCTAAGACTATTTTGGCAGAAAT  
 TCAAAATCGTACTTTGGCCATGAATTTCTGGGCAACGATAGAACATTCTCTCAACTACAAGTACCAAGGG  
 GATTTCCAGATGAGATTAAAGAGCGACTGGAAATTACAGCTAGAATCGCCATCAGTTGGATGAAGAA  
 ATGGGTGAAATTCGTGATGATATCCAAGAAGCCCAGGCACCTTTTGTATCCTTTGAGTAGAAAAATTAATG  
 ACGGTGTAGGAAACAGTGACGATACAGATGAAGAATACAGGCTCGAGCACCACCACCACCACCTGA

## 2 CFE 52 "homologue of SEQ. ID NO. 48"

Fig. 73

ATGCAACTTAATACACACAATGCTGAAATCTTGGCTCAGTGCAGCTAATAAGTCCCCTATCCGCAGGATG  
 AACTGCCAGAGATTGCCCTAGCAGGGCGTTCAAATGTTGGTAAATCCAGCTTTATCAAACTATGTTGAA  
 CCGTAAGAATCTCGCCCGTACATCAGGAAAACTGGTAAACCCAGCTCTGAACTTTTAACTTGAT  
 GACAAAGATGCGCTTTGTGGATGTGCTGTTATGGCTATGCTCGTGTCTTAAAAAGGAACGTGAAAAAT  
 GCGGGTGCATGATTGAGGAGTACTTAACGACTCGGAAAAATCTCCGTGCGGTTGTCTAGTCTAGTTGACCT  
 TCGTCAAGACCCGTCAGCAGATGATGTGCAGATGTACGAATTTCTCAAGTATTATGAGATTCCAGTCATC  
 ATTGTGGCGACCAAGCGGACAAAGATTCTCTGGTAAATGGAACAAGCATGAATCAGCAATCAAAAAG  
 AATTAAACTTTGACCCCAAGTGACGATTTCTCTCTTTTCTCTGTCAGCAAGGCAGGGATGGATGAGG  
 CTTGGGATGCAATCTTAGAAAAATTTGGCGGCCGCACTCGAGCACCACCACCACCACCTGA

## 2 CFE 53 "homologue of SEQ. ID NO. 49"

Fig. 74

ATGAAACAAGAAAAATCCCTTTGCGCAAGTCTGTTGTGTCTAACGAAGTGATTGATAAGCGTGATTGTC  
 TCCGCAATTGTCAAGAAACAAGGAAGGACAAGTCTTTATTGATCCTACGGGCAAGGCCAATGGCCCGGGCG  
 CTTATATCAAACTAGACAATGCAGAAGCCCTAGAGGCGAAAAAGAAAGAGTCTTTAACCAGCAGCTTTA  
 GCATGGAAGTGGAAAGAAAGCTTTTATGACGAGTTGATCGCTTATGTGGATCACAAGTGAAAAAGAAAG  
 AGTTGGGACTTGAACTCGAGCACCACCACCACCACCTGA

## 2 CFE 54 "homologue of SEQ. ID NO. 50"

Fig. 75

ATGTTAAACCCTCTATTGATACCTTGCTGACAAAGGTTCTTCAAATATTCACCTCGTAATCTTGGAAAGC  
 AAAACGTGCCCACGAATTGGAAGCAGGTGCCCCAGCAACTCAAGGTTTCAAGTCTGAAAAATCAACTCTT  
 CGCCTTTAGAAAGAAATCGAATCAGGAAACGTTACAATTACCCAGATCCAGAAGGAAAAACGTGAAGCA  
 GTCCCTGCGCGTATCGAAGAAAGAAAAACGCGCAAGAAAGAAAGAAAGAAATCAAGAGCAAAAT  
 TGCTAAAGAAAAAGAAAGATGGTGAAAAAATTCTCGAGCACCACCACCACCACCTGA

## 2 CFE 55 "homologue of SEQ. ID NO. 51"

Fig. 76

ATGTCAATTAACATCAAAACAACGTGCTTCTCAACAGCCAGGCCACACACCCCTCAAACCTATCATCCAAA  
 TCGGGAATAATGGACTCAACGACCAAAATCAAAACAGCCTCCGTCAAGCTCTTGATCGCGGTGAATTAA  
 TGAAGGTACTCTCTTACAAAACACAGATGAAAAATCCACGAAGTAGCTGAAATTTTGGAAAGAAAGAA  
 TCGGTGTGGATACAGTCCAAAAAATAGGACGCATCTTGATTTTGTTTAAACAATCTAGCAAGAAAGAAAA  
 TCGCAAGATTTCTAAGAAAGTCAAGAAATCTCGAGCACCACCACCACCACCTGA

## 2 CFE 56 "homologue of SEQ. ID NO. 52"

Fig. 77

ATGGCATTGAAAAATTATATACCAGATTTTGTGTGGAAGCAGTCTATGATCTGACAGTCCCAAGCCTGC  
 AGCGCAGGGAATCAAGGCTGTTTGTGTGATTGGATAATACCCTCATTTGCTTGGAAACAACCTGATGG  
 AAGGCCAGAGATGAAGCAATGGCTACATGACCTTCGGGACGCGGTATTTGGCATTATCGTAGTGTCAAAT  
 AAACCAAAAAACGCTTCAACGAGCAGTTGAGAAATTTGGGATTGATTACGTTTACTGGGCTTGAAGC  
 COTTCACATTTGGTATTGACCGTGCTATGAAGGAAATTCACATGACAAAAAGGAAGTGGTCATGGTTGG  
 CGACCACTCATGACAGATATACGAGCAGCCACCCTGCAAGGATTTCGGTCAATTTTAGTCAAAACCTTGG  
 GTCAACATGACTCAATCAAAACGACAGATTAACCGAACTCGTGAGCGTCTGTTATGAGAAAAATCACTG  
 AAAAGTACGGACCGATTACATATAAAAAAGGAATTTCTCGAGCACCACCACCACCACCTGA

## 2 CFE 57 "homologue of SEQ. ID NO. 53"

Fig. 78

ATGTTTCAAAAAATTTAATTGCCAATCGTGGTGAATTTGCGGTTCTGATTATCCGTGCGGCACGTGAATT  
 GGGGATTGGCAGCGTAGGGTTTATTCAACTGCTGATAAGGAAGCTCTCATACGCTTTTGGCAGATGAA  
 GCAATTTGTATTGGTCTGGCAAGGCAACAGAGTCTTATCTCAATATTAATGCAGTTCTATCACTGCACT  
 CTTACTGAGGAGAAAGCTATTCACCCTGGTTTGGATTCTCAGTGAAATTTCCAAATTTGCGACCATGT

2CFE 57

Fig 78 (contd)

GTGAAGAAAGTAAAGTATCAAGTTTATCGGTCCATCTGGTCATGTTATGGATATGATGGGGGATAAGATCAA  
 TCCGCTGCTCAGATGATTAAAGCAGGTGTGCTGTTATACCAGGTTTCAAGGCTTCAGATGGAGAAAGTGCATAACTCT  
 GAAGAAAGCTTTGATTGTTGCTGAAAAAATTGGCTATCCTGTTATGCTCAAGGCTTCAGCAGGTGGAGGTG  
 GTAAAGGATTCOTAAGGTTGAAAAACCAGATGACCTCGTTTCTGCTTTGAAACTGCCTCTAGTGAGGC  
 CAAGGCAATTATGGCAATGGTGCCATGTACATAGAACGGGTTATCTATCCAGCTCCGGCACATTGAGGTT  
 CAAATCCTAGTGATGAGCATGGACATGTGATTCACTTGGGTGAACGGGATTGTTCTCTTCAAAGGAAATA  
 ACCAAAAGGTTTTGAAAGAAAGTCCCTCGATTGCAATCGGAAAAACGCTGCGTCAATGAAATAGGTGCTG  
 CTCTGTTCCGAGCGGCAGAGTTTGTGGCTATGAGAATGCAGGAACCATTTGAATTTCTTCTTGATGAAGC  
 AAGTAGAAAATTTCTATTTTCATGGAGATGAATACTGTTTTCAGGTAGAACATCCAGTAACAGAGTTTGT  
 TCAGGTGTTGATATCGTTAAGGAACAGATTTGCATTGCGGCAGGTGAGCTTTGTCTGTTAAGCAAGAAAG  
 ATATTGTCCTACGCGGTGATGCCATCGAGTGTCTGATCAATGCAGAAAACCCAGCCTTTAACTTTGTCTCCA  
 AGTCAGGTAAGATTACTAACTCTATCTGCCAAGTGGTGGAGTTGGCTTGGCGTGGATTTCAGCAGTTT  
 ATCCAGGTTTAACTTCCGCTTATTATGATAGTATGATTGCCAAAATCATAGTACACGGCGAAAAATCG  
 TTTGACGCTTGATGAAAATGCAACGTGCCCTCTATGAATTAGAGATTGAAGGAGTGCAGACCAATGCA  
 GATTTCAGCTTGATCTCATTTCAGATCGCAATGTCATTGCTGGGATTATGATACCTTCTTCTTGATGGA  
 AACCTTCTTACCTAAATATCAAGAAAAAGAACTCGAGCACCACCACCACCACCTGA

Fig 79

2CFE58: "homologue of SEQ. ID NO. 54"

ATGATTACAAAGTTTTTTTATCAAGAAACAAAGAACGTAGCCCAACGCGTGAACAAACACGCACGCTTT  
 ACCTAGACATCGATGCCAGCTCAGAACTTGAGGGCGGTATCACTGCTCGCCAACTTGTGGAAGAAAAATCG  
 CCCAGATACAAATATCGAGTATATCGAACTCTTGTCTGACAAATTGCTCGATTACGAAAAAGAACTGGC  
 GCCTTCGAAATTACGGAGTTCTCTGAGCACCACCACCACCACCTGA

Fig 80

2CFE59: "homologue of SEQ. ID NO. 55"

ATGAAGGATAGATATATTTTATGACATTTGAGACATCTGTGATGAGACCAGTGTGCGCGTCTTGAAAAACG  
 ACGATGAGCTCTTGTCCAAATGTCATTGCTAGTCAAATGAGAGTCACAAACGTTTTGGTGGCGTAGTGCC  
 CCAAGTAGCCAGTCGTACCATGTGCGAGGTCAATACAGCCTGTATCGAGGAGGCATTGGCAQAAAGCAGG  
 GATTACGGAAGAGGACGTGACAGCTGTTGCGGTTACCTACGGACCCAGGCTTGGTCCGAGCCTTGTCTAGTT  
 GGTGTTGTCAGCTGCCAAGGCCCTTGTCTGGGCTCACGGACTTCCACTGATTCCCTGTTAATCAATGGCTGG  
 GCACCTCATGGCAGCTCAGAGTGTGGAGCCTTGGAGTTTCCCTTGCTAGCCCTTTAGTCAAGTGGTGGC  
 ACAAGAGTTTGTCTATGTTTCTGAGGCTGGCAATTACAAGATTGTTGGGGAGACACCGAGACGATGCACT  
 TGGGAGGCTTATGACAAGGTCGGTCTGTGATGGGCTTGACCTATCCTGCAGGTCGTGAGATTGACGAG  
 CTGCTCATCAGGGGCAGGATATTATGATTTCCTCCGTCGCATGATTAAAGGAAGATAATCTGGAGTTCT  
 CCTTCTCAGGTTTGAATCTGCTTTATCAATCTTCAATCAATGCGGAGCAAAAGGGAGAAAGCCTGTC  
 TACAGAAAGATTGTTGTGCTTCTTCCAAGCAGCAGTTATGGACATTCTCATGGCAAAACCAAGAGGCT  
 TTGGAGAAATATCCTGTTAAACCCCTAGTTGTGGCAGGTGGTGTGGCAGCCAATAAAGGTCTCAGAGAAC  
 GCTAGCAACTGAAATCAGAGATGTCAATGTTATCATCCACCTCTGCGTCTGTGGGAGACAATGCAAG  
 TATGATTGCTTATGCCAGTGTGAGCGAGTGGAAACAAAGAAACTTTGCAAACTTGGACCTCAATGCCAAA  
 CCAAGTCTTGCCTTTGATACCATGGAACTCGAGCACCACCACCACCACCTGA

Fig 81

2CFE60: "homologue of SEQ. ID NO. 56"

ATGTGTGAATTTGTTGGTGTGTTGGAAAACAAAAAGCAACTGATATTTTGATTCAAGGGCTTGAAAAAGC  
 TTGAATACCGTGGCTATGATTCTGCGGGAATTTTGTCTAGATGGTGTGATAACCATTTGGTGAAGGCT  
 GTTGGTCTATGCGCAAAATTTGCTGCCAAGACAGCTGGTGTGAGGGAACAACTGGTATCGGACATACTC  
 GTTGGGCAACTCATGGGAAACCAACGGAAGACAATGTCTACCCACACCGCTCTGAGACAGAACGTTTTG  
 TCTTGGTTCAAAATGGGTGATTGAAAACTACCTTGAAATTAAGAAAGAAATACCTTGTGGGCACCACTT  
 CAAAGGCAAAACAGATACGGAATCGCCGTACATTTGATTGAAAAATTTGCGGAAGAAAGACCGTCTCTC  
 AQTCTTGAAGCCTTTAAAAAAGCTCTTCATATTATCCGTGGTTTCATATGCCCTTTGCCTTGAATTGACTCTG  
 AAAATCCAGATGTCATCTATGTAGCGAAAAACAAATCTCCACTTTTGATTGGTCTTGGGGAAGGCTACAA  
 TATGCTCTGCTGAGATGCTATGGCTATGATTGCTGAAACCAACCAATACATGAAATTCATGACCAAGAG  
 TTGTAATCGTCAAGGCTGATAGCGTGGAAGTTCAAGACTATGATGGTAACAGTCTGTAACGCTGCTAGCT  
 ATACTGCGGAACCTTGACTTGTGAGATATCGGTAAGGGAACCTTATCCTTACTACATGCTTAAGGAAATGGA  
 TGAGCAACCAACTGTTATGCTAAACTCATTCAAGCCTACACGGATGATGCTGGTCAAGTAGTGATTGAT  
 CCTGCTATCATTAAGGCTGTTCAAGACGACAGCCGATCTACATCCTTGCAGCTGGAACATCTTACCATG  
 CAGGATTGCTTCAAGAAAAATGTTGGAAGAATTGACAGATACACCAAGTTGAACTTGGCATCTCATCTGA  
 GTGGGGCTACGTTATGCCACTTCTCAGCAAGAAACCACTTTCATCTTTATCAGCCAATCTGGTGAACA

2 CFE 60 (contd.)

Fig 81 (contd.)

GCGGATAGTCGTCAAGTTTTGGTCAAGGCTAATGAAATGGGAATTCCAAGCTTAACAGTGACAAACGGTTC  
 CAGGTTCAACCCCTCTCAGTGAAGCCAATACCATGCTCCTTEACGCAGGTCCGTGAAATTGCCGTGGC  
 ATCAACTAAAGCCTATACAGCGCAAATCGCAGCCCTTGCCCTTCCTTGCAAAAGCAGTCGGAGAAGCAAAT  
 GGTAAITGCTAAAGCGCAAGCCTTTGACCTGGTTTCATGAATTGTCAATCGTAGCTCAGTCTATCGAATCAA  
 CTCTTCAGAGAAAAGAAACCATTAAGCCAAGGTTCTGTGAACCTCTTGAAACAACCTCGTAACGCCCTTTTA  
 CATCGGACGTGGTCAAGATTACTACGTAGCCATGGAAGCAAGTCTCAAACCTCAAAGAGATTTCTTATATC  
 CAGTGTGAAGGTTTTGCGGCAGGAGAACTCAAGCACGGAACCATTTGCCCTTGATTGAAGAAGGAACACCT  
 GTCTTGCTGTCTGTGATCCAGTCCCTTGCCAACCACTCGTGGAATAATCCAAGAGGTGGCAGCCC  
 GTGGTCTAAGGTCTCACTATCGCAGAAAGAAATGTTGCTAAAGATAACCGACGATATCGTCCCTACGAC  
 TGTACAACCTTACCTCTACCAATTTCAATGGTCTGACCGACGCAATTTGGTTGCTTACTTTGCAACCCCTCC  
 ACCGTGGCTCGATGTGGATAAACCACGTAACCTTGCCAAGTCAGTAACGGTAQAACCTCGAGCACCACC  
 ACCACCACCACTGA

Fig 82

2 CRE61 "homologue of SEQ. ID NO. 57"

ATGATACGTATCGAAAATCTCAGTGTCTCTACAAAGACACGTTGGCACTTAAGGATATTTCACTAGTGC  
 TCCATCGACCAACAATTACCGGCATCATTTGGTCCAAACGGCGCTGGGAAATCAACACTATTAAAAAGGTAT  
 GGTGGGAATTAATCCACATCAAGGTCAGGCATTTCTCGATGACAAGGAAGTTAAAAAATCCTTACCCGA  
 ATTGGCTATGTGCAACAAAAATCAATATCGACTACAACCTTTCCCATCAAGGTCAAGGAAGTGGCAAGAGGC  
 TAGGACTATTTCCCTCTATTCCCTCTTTTCGAAGTTAAAGGCTAAACATTGGAAGAAAGTGAAGAGGC  
 CCTTGAATCGTGGCCTAGCTGACTACGCTGAACGTCAAATTAGTCAACTGTCTGGAGGTCAATTCAG  
 CGGTTTTGATTGTCAGATGTTTGTGTCAGGAAGCCGACTATATCCTCTTGGATGAACCCCTTTGCTGGGAT  
 TCACTGTCTCAGTGAGGAAATCATCATGAATACGCTGAGAGATTGAAAAAAGCTGGGAAGACGGTTCT  
 CATCGTTACACGACCTCAGCAAGATTCCCACTACTTCGATCAAGTCTTACTTGTCAATCGAGAAGTG  
 ATTGGCTTTGCTCCAACAAAGAAACTTTTACCGAAACCAATCTAAAAGAAAGCTTACGGTAATCAACTCT  
 TTTCAATGGAGGTGACCTACTCGAGCACCACCACCACCACCACTGA

Fig 83

2 CRE62 "homologue of SEQ. ID NO. 58"

ATGCCGAAAGAGTGAATTTAACAGGCGAAGAAAGTTGTCGCTTTAACCAAAGAATATTTAACGGAAGAG  
 GATGTTCATTTTGTCCATAAGGCCTTGGTCTATGCTGTTGAATGCCACAGTGGTCAATATCGCAATCAGG  
 CGAGCCTTATATCATTACCCCTATCCAAGTGGCAGGTATTTTAGCTAAGCTAAAGCTGGATGCTGTAAACA  
 GTAGCTTGTGGAATCTTGCATGATGTTGGTGAAGATACAGATGCGACTTTGGACGATTTGGAAAGAGAGT  
 TTGCTCTGATGTGCGGATGATTGTTGACGGAGTTACCAAGCTTGGCAAGGTCGAGTACAAATCGATCGA  
 GGAGCAATTAGCGGAAAAATCATCGCAAGATGCTCATGGCCATGTCTGAGGACATCCGCTTATTTGCTC  
 AAAGCTGTGACCGCTTGCACAATATGCCGACCCCTGAAACATCTTCGAAAAGACAAGCAGGAGCGTATTT  
 CCAAGAAACCATGGAATCTATGCCCGGCTTGCCTATCGTTTGGGGATTTCAGTGTCAAATGGGAATT  
 AGAAGACTTGTCTTTCCGTTATCTCAATCCAACGGAGTTTACAAGATTACCCATATGATGAAGGAAAAAG  
 CGCAGGAGCGGTGAGGCTTGGTGGATGAGGTAGTCAACAAATTAAGAGGAGTATACGACAGAACCTCAC  
 TTGAAAGGGAAGATTTATGGTCTGCCAAGCATATTTACTCAATTTCCCGCAAAATGCAAGCAAGAGAA  
 AACCGTTTGAGGAAATCTATGATCTGATTGCTATTCGTTGATTTTAGATACCCAAAGTGATGTTTATGCC  
 ATGCTTGGTTACGTGCATGAATTTTGAACCCGATGCCAGGTGCTTCAAAGACTATATCGCCAACCGCA  
 AGGCCAATGGTTATCAGTCTATCCATACGACTGTTTATGGACCAAAAGGCGGATTTGAATTCAGATTCC  
 AACCAAGGAAATGCAAGAGGTGGCTGAGTACGGGTTGCGGCTCACTGGGCTTATAAGAAAGGTATAAA  
 GGGCAAGTTAACAGCAAGGAATCAGCTATTGGAATGAAGTGGATCAAGGAGATGAGGCTCAAGA  
 CCAGGCTGATGATGCTAAGGAATTTGTGGACTCTGTTAAGGAAAACTATTGGGTGAGGAGATTACGTT  
 TTTACCCAGATGGAGGTGTCCGTTCCCTTCCCAAGATTACAGGACCGATTGATTTTGCTACGAAATCCA  
 TACCAAGGTCCGTTGAAAAAGCAACTGGTGCCAAGGTCAATGGCCGATGTTTCCACTGACAACCAAGTT  
 AAAGACAGGGGATCAGGTTGAAATTAAGCCAACCCGAACCTCTTGGACCTAGCCGTGACTGGCTCAAT  
 ATGGTCAAGACTAGCAAGGCGCGCAATAAGATTGCGCAGTTCTTAAAAACCAAGATAAGGAATTTGCT  
 GTCAACAAGGTCGTGAGATGCTGATGGCTCAGTTCCAAAGAAAAATGGCTATGTGGCAAAATAATTTATGG  
 ACAAGGCCACATGGATCAAGTTCTGCAAAAGACCAGTTACAAGACAGAAAGACTCCCTCTTTGCGGCCAT  
 TGGTTTTGGGAAATCGGTGCGATTACCGTCTTTAACCGTCTGACTGAAAAAGAGCGCGCTGAGGAAGAG  
 CGTGCCAAGGCCAAGGCTGAGGCAGAGGAGCTTGTCAAAGGTGGCGAGGTCAAGGTTGAAAAATAAAG  
 AACTCTCAAGGTCAAGCATGAGGGGGAGTGGTTATTGAAGGTGCTTCTGGTCTCCTAGTGGGATTGCT  
 AAGTGTGTAAACCCCGTGGCTGGTGACGATATGTTGGCTACATTACCAAGGGTCTGTGTGGCTATTC  
 ACCGTGTGACTGTATGAACCTGCGTGCCCAAGAAAACTACGAGCAACGTCTCCTTGTATGTGAATGGGA  
 AGACCACTACTCTAGCTCAAATAAGGAGTATATGGCCATATCGATATCTACCGTCTCAACCGTACAGGA

2 CFE 62 (contd)

(Contd)

Fig 83

CTGTGAAACGATGTACTGCAAGTTCTTTCAAATACAACCAAGAATATTTCAACGGTCAATGCCCAACCAA  
 CCAACGATATGAAGTTTGCTAATATCCATGTGTCTTCGGTATTGCCAACCTCTCTACACTGACCAACGGTT  
 CTCGATAAAATTAAGAGTGTGCCAGAGTTTACTCTGTCAAACGGACCAACGGCCTCGAGCACCACCACC  
 ACCAACCCTGA

2 CFE 64 "homologue of SEQ. ID NO. 60"

ATGACAGAAAGAAATCAAAATCTGCAGGCACAGGATTATGATGCCAGTCAAAATTCAAGTTTTAGAGGGC  
 TTAGAGGCTGTTCGTATGCGTCCAGGGATGTACATTGGATCAACCTCAAAAGAGGTCTTCACCATCTAG  
 TCTGGGAAAATTGTTGATAACTCAATTGACGAGGCCCTTGGCAGGATTGGCCAGCCATATTCAAGTTTTTATT  
 GAGCCAGATGATTGCGATTACTGTTGTGGATGATGGGCGTGGTATCCAGTCCGATATTGAGGAAAAACAG  
 GTCTGCTGCTGTTGAGACCGTCTTTACAGTCTTTCACGCTGGAGGAAAGTTCCGGCGTGGTGGATACAA  
 GGTTCAGGTGCTCTTCACGGGGTGGGGTCTGTCAGTTGTTAATGCCCTTTCCACTCAATTAGACGTTTCATG  
 TCCATAAAAACGGTAAGATTTCATTACCAAGAATACCGTCTGGTTCATGTTGTGCGCAGATCTTGAAATAGT  
 TGGAGATACGGATAAAACAGGAACAACTGTTCACTTACACCGGACCCAAAAATCTTCACTGAAACAAC  
 AATCTTTGATTTTGATAAAATTAATAAAACGGATTCAAGAGTTGGCCTTTCTAAATCGCGGTCTTCAAATTT  
 CTATCACTGATAAGCGCCAAGGTTTGGAAACAAACCAAGCATTATCATTATGAAGGTGGGATTGCTAGTTA  
 CGTTGATATATCAACGAGAACAAAGGATGTAATCTTTGATACACCAATCTATACAGACGGTGAGATGGAT  
 GATATACAGATTGAGGTAGCCATGCAATACACAACGGGTIACCATGAAAAATGTCATGAGTTTCGCCAATA  
 ATATTGATACACATGAAGGTGGAAACGATGAACAAGGTTTCCGTACAGCCTTGACACGTTTATCAACGA  
 TTTAGTCTGTAAGAATAAGTTACTGAAAGACAATGAAGACAATCTAACAGGGGAAGATGTTCCGGAAGG  
 CTAAAGTCAAGTTATCTCAGTTAAACACCCAAATCCACAGTTTGAAGGACAAACGAAGACAAATTTGGGA  
 AATAGCGAAGTGGTCAAGATTACCAATCGCCTCTTCAGTGAAGCCTTCTCCGATTTCCTCATGGGAAATC  
 CACAGATTGCCAAACGTATCGTAGAAAAAGGAATTTTGGTGGCAAGGCTCGTGTGGCTGCCAAGCGTGC  
 GCGTGAAGTCAACGTAAAAAATCTGGTTTGGAAATTTCCAACCTTCCAGGGAAACTAGCAGACTGTTCT  
 TCTAATAACCCCTGCTGAAACAGAACTCTTCATGCTGGAAGGAGACTCAGCTGGTGGATCAGCCAAATCTG  
 GTCGTAACCGTGAGTTTCAAGCTATCCTTCCAAATTCGCGGTAAAGATTTTGAACGTTGAAAAAGCAAGTAT  
 CGATAAGATTCTAGCTAACGAAGAAATTCGTAGTCTTTTACAGCCATGGGAACAGGATTTCGGCGCAGAA  
 TTGATGTTTTGGAAGCCCGTTACCAAAAATCTGTTTGTATGACCGATGCCGATGTGATGGAGCCACCA  
 TTCTGATCCCTTCTTTTAAACCTTGATTATCGTTATATGAAACCAATCTTAGAAGCTGGCTATGTTTATATTG  
 CCCAACCACCAATCTATGGTGTCAAGGTTGGAAGCGAGATTAAAGAAATATATCCAGCCGGGTGCAGATC  
 AAGAAATCAAACTCCAAGAGCTTTAGCCCGTTATAGTGAAGGTCTGACCAACCGACTATTCAGCGTTA  
 TAAGGGGCTAGGTGAAATGGACCATCATCAGCTGTGGGAAACAAACCATGATCCCGAACATCGCTTGAT  
 CGCTAGAGTTTCTGTAGATGATGCTGCAGAAAGCAGATAAAATCTTTGATATGTTGATGGGGGATCGAGTA  
 GACCCCTGTCGTGAGTTTATCGAAGAAAAATGCTGTCTATAGTACACTTGATGTCCTCGAGCACCACCACC  
 ACCAACCCTGA

Fig 84

2 CFE 65 "homologue of SEQ ID NO. 61"

ATGGGATTACTGAAGAAACAGTACGTTTAAATTTGGACGATTCCAATAAAAAAGAAATTAGCGAAAACCT  
 TGCAGATGTTTATGCTTCGTTGAACGATAAGGGTTACAACCCCAATTAACCAAAATCGTAGGTTACGTATT  
 GAGTGGAGACCCCTGCTACGTTCTCGTTATAATAATGCACGAAATCAAATCCGTAAGTATGAGCGTGAT  
 GAAATCTTTGAGGAATTGGTTCTGCTACTATCTCAAAGDACAAGGATCGATCTACTCGAGCACCACCACC  
 ACCAACCCTGA

Fig 85

2 CFE 66 "homologue of SEQ. ID NO. 62"

ATGGTCAACTATCCACATAAAGTTTCATCACAAAAAGACAAACATCTCTTTCTCAACCCAAAAATTTG  
 CAAATCGAGGAATGTCTTTGAAAAGATGATCAATGCTACCAACGACTACTATTGTTCTCAGGGCTTGGC  
 TGTATACATAAGAAACCAACTCTATTCAAATCGTACAAGTGGACTATCCACAACGAAGTCGTGCCAAG  
 ATTGTTGAAGCCTATTTTCGACAAGCTTCAACGACGGAATTTCTGGCGTTTATAATGATATTACATCGA  
 CTGTTGAAGTCAAGGAAACAAACAAACAGTGGGATTCCGATGAAAAATTTTCATCCACATCAGATTCA  
 CATATGGAACAAGTCTTGCCEAAACAAAGGAATCTGCTTTGTCCTTCTCACTTTTCTCTCAGCAAGAAAC  
 CTACTTATGCGCGCATTGATTTGATTCGCTTCTATCATCAAGATAAGGGACAAAAATCAATGCCACTTO  
 AATATATTCGAATAATATGATATGAAATCAAGGCTGGTGCCTTCCCTCAAATTCCTTATCTCAATGTTATC  
 AAAGAAGATTTATTAGGTGGTAAAAACAAGACTCGAGCACCACCACCACCACCCTGA

Fig 86

2 CFE 67 "homologue of SEQ. ID NO. 63"

2 CFE 67 homologue of SEQ ID NO: 63

ATGGCTTATTTAGTAAAAAGATAAGTATATTCGAATCAATCCCAATCGTTCGGTTAGGGAAAAACCTC  
AAGCTAAGCCAGAGGTTCCAGATGAATTATTTTCCAGTGTCAGGCTGTAAGCATACCATCTATCAGAA  
GGATCTGGGAAGTGAAACGTATCTGTCCGCACTGTAGCTATACCTTTCTGATTTCTGCCCAAGAACGCTTGG  
CTTTACGATTOATATGGGAACCTTCAAAGAATTGTTTACAGGGATTGAAAGCAAGGATCCCTTGCATTT  
CCCTGGTTACCAAAAAGAACTGGCATCTATGCGTGAAAAAACAGGTCTGCATGAAGCCGTTGTGACAGG  
AACTGCTCTTATTAAGGTCAAGACTGTGGCTCTTGGGATTATGGATTCTAATTTATCATGGCTTCTATGG  
GTACGGTTGTAGGTGAAAAAATCACTCGTTTGTGAGTATGCGACTGTGAAAAATTGCCAGTTGTCTCT  
ATTCACAACCTCTGGTGGAGCCCGTATGCAAGGAAGGAATCATGAGTCTCATGCAAGTGGCTAAGATCTCT  
GCAGCGTTAAACGCCATTCAAATGCTGGTCTCTTTACCTGACCATTTTGACAGATCCAAACGACTGGTG  
GTGTGACGCTTCTTTCCGCTATGGAAGGCGATATCATTTCTGGCTGAACCACAGAGCTTGGTTGGTTTGGCT  
GGCGCTGTGTGATTGAAAAATACGGTTCGTGAAAGCTTGCCTGAGGATTCCAAAAGGCAGAAATTCCTAT  
TAGAATATGGCTTTGTGGATGCTATTGTCAAAAAGAGAGACTTACCAGATACGATTGCTAGCCTAGTCAG  
ATTGCATGGAGGGAGTCTAGACTCGAGCACCACCACCACCACCTGA

2 CFE 68 "homologue of SEQ. ID NO. 64"

ATGAGATTATGGGATTGGACGTCGGTTCAAAAACGGTAGGGGTGGCGATTAGCGATCCGCTTGGTTTTA  
CAGCTCAGGGCTTGAATCATCCAGATAAATGAAGAACAAGGCCAATTTGGTTTTGACCCGCTTAAGG  
AATGGTTGATACCTACAAGGTGGAACGATTTGTAGTGGGCTTGCCTAAAAACATGAACAATACAAGTGG  
ACCGCGCTAGAAGCTAGTCAAGCCTACGGAGCAAAGCTAGAAGAGTTTTTGGTTTACCAGTAGACTAT  
CAGGATGAACGCTTGACAACAGTGGCTGCTGAGCGCATGTTGATTGAACAAGCAGATATCAGTCGCAAT  
AAGCGCAGAAAGTCAATTGATAAGTACAGCTCAGCTGATTTACAAAATTATTAGATAGAAAAATTC  
TCGAGCACACCACCACCACCACCTGA

2 CFE 69 "homologue of SEQ. ID NO. 65"

ATGACAAAACCTTACTGTTAAAGACGTTGACTTGAAAGGTAAAAAGTCTCTCCTTCTGTTGACTTCAACG  
TACCATTTAAAGATGGCGTAATCACTAACGATAACCGTATCACAGCAGCTCTTCCAACCTAATAAGTACAT  
CATCGAAACAAGGTGGACGTTCAATTTCTTCTCACCTTGGACGTTGAAAGAAGATCTGATAAAGCT  
GGTAAATCACTTGTCTCTGTAGCAGCTGACTTGGCAGCAAAACTTGGTCAAGATGTTGTTTCCAGGTGT  
CACTCGTGGTGTGTAATTGGAAGCGGCAATCAAACGCTCTTGAAGATGGACAAGTTCTCTTGGTTGAAAAAC  
ACTCGTTACGAAGATGTTGACGGCAAGAAAGAAATCTAAAAACGATCTGAACTTGGTAAATACTGGCA  
TCATTGGAGATGGTATCTTGTAAACGATGCAATTCGGTACAGCTCACCGTGCACAGCATCTAACGTTG  
GTATCTCAGCAACGTTGAAAAAGCAGTTGCTGTTTCTTCTTGAAGAACGAAATTGCCATACATCCAAGA  
AGCAATTTGAAACTCCAGAACGTTCCATTCCTGGCTATCCTTGGTGGTTCAAAAAGTTTCAGACAAGATCGGT  
GTATCCAAAACCTTCTTGAAGAAAGCTGATAAAGTCTTATCGGTGGTGGGATGACTTACACATTCTACA  
AAGCACAAGGTATCGAAATCGGTAACTCACTTGTAGAAGAAGACAAATTGGATGTTGCGAAAGCTCTTCT  
TGAAAAAGCAAAATGGTAAATTTGATCTTGCCAGTTGACTCAAAAGAAGCTAACGCAATTTGCTGGTTACACT  
GAAGTGGGTGACACTGAAGGTGAAGCAGTTTCTGAAGGCTTCTTGGTCTTGACATCGGTCCAAAATCTA  
TCGCCAATTTTACGAAGCTTTGACTGGTGCCAAAACAGTTGTATGGAACGGACCTATGGGTGTATTTGA  
AAACCCAGATTTCCAAGCTGGTACAAATCGGTGTGATGGACGCTATCGTGAAACAACAGGAGTTAAATC  
AATCATCGGTGGTGGTGACTCAGCTGCCGACGCAATTAACCTTGGCCGTGCAGACAAGTTCTCATGGATT  
AGTAGGGGTGGTGGAGCATCAATGGAACCTTCTTGAAGGTAAAGTTCTTCCAGGACTTGCAGCCCTTGACAO  
AAAAACTCGAGCACACCACCACCACCACCTGA

2 CFE 70 "homologue of SEQ. ID NO. 66"

ATGTTAAATCAGAAAAACAATCAGTTATCAAATGTTAAATGAAGAATTGTCCTTCTTATTGGAAGGCG  
AAACCAATGTTTGGCTAATCTTTCCAACGCCAAGTCTCTCATAAATCAGCTTTTCTTAATACCGTATTT  
GCAGGCTTTTATTTGTTGATGGAAGGAATTTGGTTTATAGGCCCTTCCAAGGAGGTGTTTCTGTCATCCG  
TATGCACTAGGCAAGGTTGTTTGGTGGAGGCACTTTCAGGAAACTGTTATTGTTGGAGATGTG  
ACCACTATCTCAACTATATTTCTGTGATAGTCTAGCTAAAAGTGAATTTGTTGGTGGCGATGATGAAGA  
ATGGTCAATTAATGGAGTTCTGGATCTGGATTCTTCAGAGATTGAGGATTACGATGCTATGGATCCGAGA  
TTATTTGGAACAATTTGCTGCTATTTGCTTGAAGACAACATGGGACTTTACGATGTTGAGGAAAAA  
TCTCTCGAGCACACCACCACCACCACCTGA

2 CFE 71 "homologue of SEQ. ID NO. 67"

ATGAGAAATCGAACTATTGACTCCCTTTACCAAGGTAGAGTTGGAGCCAGAAATCAAGGAGAAAAAACGC  
AAACAAGTTGGGATTTTAGGGGGGAATTTTAAACCTGTTCACAATGCCCATCTCATTTGTCGGATCAAG

2 CFE 71 (Contd.)

Fig 91 (Contd.)

TACGGCAACAGTTGGGACTGGATCAAGTCTCTCATGCTGAATACCAACCTCCTCACGTTGATAAAAA  
 GQAAACCATCCCTGAACACCATCCTCTCAAGATGCTTGAGTTGGCAATTGAGGGGATTGACGGCCTAGTC  
 ATTGAAACCATTTGAGTTGGAGCGCAAGGGTATTTCTACACCTACGATACCATGAAGATTTTGACAGAGA  
 AGAATCCAGATACGGATTATTACTTTATCATCGGTGCCGACATGGTTGACTATCTGCCTAAGTGGTACCG  
 AATTGATGAACCTGGTTGACATGGTTCACTTTGTGGGGGTTTCAGCGTCCACGCTACAAGGTAGGGACTTCC  
 TATCCAGTTATCTGGGTGGACGTACCGCTCATGGATATCTCGTCCAGCATGGTGGGGGACTTCTTGGCCA  
 AGGTCCGAAACCCAACTTTCTCTACCTCAGCCAAGTGCTAGACTACATCGAGAAGGAGGGGCTCTACCTC  
 GAGCATCACCAACCACCACTGA

2 CFE72 "homologue of SEQ. ID NO. 68"

Fig 92

ATGAAATTGCAAAAAATAGTCAAGAGAAGCGCGTGAACAGAGTCGCTTGACAACCTTGGACTTTGGGACA  
 GGCATTTTGTATGAATTTATCCAATTACATGGTGACCGTTCTTTTCGTGATGATGGTGCACTTGTGGTGG  
 TATTGGTTGGCTTGGAGACCAAGCTGTAAACAGTGGTTGGTATCCAAAAAGGCAAGAGTTTGCAAGACAA  
 COTCAAACGGAATTTGGCCAAACCACATCCAGAAAGCTACCGAAAGGCACTGCGGTTGATGAACACGGC  
 TGAGAATTGGCCGTCCAGTTGTGACCTTTATCAATACAGCAGGTGCTTATCCTGGTGTGGAGCGGAA  
 QAACGTGGTCAAGGGGAAGCTATCGCTCGCAATCTCATGAAAATGAGTGACCTGAAAGTCTCTATTATCG  
 CCATTATATCGGTGAAGGTGGTTCAGGCGGGGCTCTGGCTCTAGCTGTGCGGACCGTGTCTGGATGCT  
 GGAATAATCTATCTATGCCATTCTCAGTCCAGAAGGCTTTGCTTCCATTTTATGGAAGGACGGTACTCGCG  
 CCATGGAAGCAGCAGAACTGATGAAAACTACTTCGCATGAACTGTTAGAAATGGACGTGGTGGATAAGG  
 TGATTTCTGAAGTAGGACTTTCTAGTAAAGAACTAATTAAGAGTGTCAAAAAAGAACTCCAAACCGAGCT  
 GGCTAGACTTTTCAAAAAACCGCTAGAAAGAGTTGCTGGAAGAACGCTATCAACGATTTAGAAAAATACCT  
 CGAGCACCAACCAACCACCACTGA

2 CFE75 "homologue of SEQ. ID NO. 71"

Fig 93

ATGTCAATAAGATTGGCTTATTCACAGGCTCATTTGATCCGATGACAAATGGGCATCTGGATATCATTG  
 AACGGCGAGCAGACTTTTGTATAAGCTTTATGTGGGTATTTTAAATCCCAACAAACAGGATTTCTT  
 CCTATCGAAAAATCGTAAACGGGGGCTAGAAAAAGGCTTTGGACATCTGGAAAAATGTTGAAGTCGTGGCT  
 TCTCATGATGAATTGGTGGTCCGATGTTGCAAAAAAGATTGGGTGCTACTTGTCTAGTGCGTGGTTGAGGA  
 ATCGGTGGGATTTGCAATATGAAGCCAGTTTGTATTACTACAATCATCAGCTGTCTCTGATATAAGAGCT  
 ATTTATTTACATAGTGACCTGAACATCTCTATATCAGTTTATCAGGCGTTAGAGAGCTTTTGAAGTTTGG  
 TCAGGATTTGCGCTGCTATGTTCCCGAGAGTATTTGGAGGAAAGCGGCGGCACTCGAGCACCACCACCAC  
 CACCACTGA

2 CFE76 "homologue of SEQ. ID NO. 72"

Fig 94

ATGACGATTTTGTGTTGTTATCAGTGCTTCTTTCTGTATATGGTTTCTCTTAGCATGAAACCCCTATCAA  
 ACAGCTAAAAAGTGAAGGAGAAAAATTAGCTCAGCAGTATGCAGGATTAGAGCAGGCTGATCAGGTTGAT  
 TTATACAAATGGCTTGGAACTTTATTACAGCGTCTTGGTCTGTAATAACAGCAAOAAGCGCTTGTCTCT  
 GATTGGTAAAGATGACCATAAGATTTACGTTTATCAGCTAAATCAGGGTATTTCAAGAAAGGAGCA  
 AACGGTTCTAAGGAAAAAGGAGCTGGCQAGATTGACAAGATAACCTTTGGTCTGTTATCAAGACAAGCC  
 AATCTGGGTAGTTAAGTCAGGATCTGATTTTATCTAGTAGATTTTGAACAGGAGCATTTGGTCAACAAG  
 GAGGGCTACTCGAGCACCACCACCACCACCTGA

2 CFE78 "homologue of SEQ. ID NO. 74"

Fig 10

ATGTTTCAATCGATAAAGAAAAATTTCACTTTGTAACCGTGACGATTTTGCCTCTGAAACTATTGATG  
 CGCAGGATATTCTTACTGGAATCAGTGTGTTAAACAATTTATGAAGAAAAATCAACTGTAGTCATGTT  
 GGOAATCTTGGTAGCCATCATTTTGATAAGTTTCTATCCCAATGTTTTCTAAGTTTGATTTCAATGATG  
 TCAGCAAGGTAAACGACTTTAGTGTTCGTTATATCAAGCCAAATGCGGAGCATTTGGTTGGGTACTGACAG  
 TAACGGTAAATCGCTCTTTGACGGTGTCTGGTTCGGAGCTGTAACTCCATCCTCATTTCTGTGATTGCGA  
 CAGTGATTAACCTGGTTATCGGTGTTTTTGTGGGTGGTATTTGGGGTATTTCAAAATCAGTTGACCGTGT  
 ATGATGAAGTTTACAACGTCTCTCAACATCCACCTCTTTGATTGTTATTGTTCTGACTTACTCAAT  
 CGGAGCTGGATTCTGGAATCTGATTTTGGCATGAGCGTAACAACATGGATTGGTATTGCTTCAATGATCC  
 GTGTGCAAACTTTGGCTATCGTGACTTGGAAATACAACCTTGGCGTACGTACTTTGGGAACACCAACCTT  
 GAAGATTGTTGCCAAAAATATCATGCTCAATGGGTATCTGTTATTGTGACAACCATGACTCAAAATGCTTC  
 CAAGCTTTATCTACATACGAAGCCTTCTGTCTTCTTCTGGTCTTGGATTACCGATTACAGTGCCAAAGTTG  
 GGTGTTTGAATTCGGATTATTCACAAAAACGTAACAACCAATGCTTACTTGTCTGATTCCATTGACAAC



(Contd.)  
Fig 95

2 CFE 78 (Contd.)

CCCTGGTCTGGTATCCTTGTCCCTTTTCGTAGTTGGTCAAAACTTAGCGGATGCTAGTGATCCACGTACAC  
ATAGACTCGAGCACCACCACCACCACCACCTGA

2 CFE 79 "homologue of SEQ. ID NO. 75"

ATGTATAACCTATTATTAACCATTTTATTAGTATTATCTGTTGTGATTGTGATTGCAATTTTCATGCAACCA  
ACCAAAAACCAATCCAGCAATGTATTTGATGCCAGTTTCAGGTGATTGTTTGAACGCAGTAAAGCTCGCG  
OTTTTGAAGCTGTAATGCAGCGTTTGACAGGGATTTTAGTCTTTTCTGGCTAGCCATTGCCTTAGCATTG  
ACGGTATTATCAAGTAGACTCGAGCACCACCACCACCACCACCTGA

2 CFE 80 "homologue of SEQ. ID NO. 76"

ATGTTTGTAGAAATAAATTATTTTGGACCACAGAAATTTACTCTTAACCATCATCTTTTACCTATGG  
AGACAGATGGGATCTTTGATTAAACCTTTTGTAGCGTGCTTAATACAATTATGATTCCATTTTATTAGG  
GGGCTTTCTTTATTATTGACAAACCTATTGTTACTTTCTTAAATAAAGTCTGTAAACTCAATCGTTTGGT  
TGGTATTTAAATTACCTTGTGACTTTGGTCTGGGGAATGGTCATAGGTGTTGCTATCTCTTACCTATTTT  
GATTAACTAGTTATCTAGTTTGATTATATCTAGTCAAACCTATTTATAGTCGAGTACAAGACTTAATCATAG  
ACTATGTAATTATCCTGCGCTCCAGAATTTGGATGTAGAAGCTACAATTCAGCAGTTAACTTATCCTAT  
GTTGATTTCTTCAAATATCCTAAATAGCGTATCAAATAGTGTGGGGAGCGTCTTGTGAGCTCTTATCAG  
TACTGTTTGAATTTGATTATGACTCCAGTTTTTTGGTTTATTTCTTATTAGATGGACATAAATCTTGGCC  
ATGCTTCAAAGAACGATTCTAAAGAGGGATCGCTTGCATATTGCAGGCTTATTAAGAATTTAAATGCGA  
CGATTGCTCGGTATATTAGTGGAGTTTCGATTGACGCAATCATTATAGTTGTTGGCTTATATTGGCTAT  
AGTATTATTGGTTTAAATATGCTTTAGTTTGTCCATTTTCTGGTGTAGCCAATTTAAATCTTATGTTG  
GGCCAAGTATTGGTTGATTCTATGATCATCGCAATATATTCACTGATCCCATAGACTGCTGATTGC  
AGTGATTATATGCTTGTGTTGACGAGGTAGATGGCAATATCTTATATCCTCGAATTTGAGGAAGTGTTA  
TGAAGTTTCATCCCAATCAGATTTTAGTTTACTTTTGTGTCAGCAATATCTATGGTGTAGTTGGAATG  
ATTGTCAGTGGCAACCAATTTCTATCTTGAAGAAATTTCTAAGTTCTTATCCCTTTGTATGAAATCA  
TAAATAATGAAAGAACGAGAAAGAGAATTAGCTAAGCTCGAGCACCACCACCACCACCACCTGA

2 CFE 81 "homologue of SEQ. ID NO. 77"

ATGTATTAAGCACTTTATCGAAATATAGAAGTCAAAACTTCTCCAGTTAGTTGGTCAAGAAGTTGTGG  
CTAAGACTCTTAAACAAGCGGTGGAGCAAGAGAAATAAGTCACGCTTATCTTTTCTGGTCCCTCGTGG  
AAGGGGAAAAACCAAGTGTGCTAAAATCTTTGCCAAGGCTATGAACTGTCCCAATCAAGTGGGTGGCGA  
ACCTTGAATAAAGTCTATATTGTCAAGCAGTGACGGACGGTAGTTTGAAGATGTCATTGAAATGGAT  
GCAGCTCTAATAATGGGGTAGATGAAATTCGCGAAATTCGTGATAAATCTACCTATGCGCTAGCCTTG  
CTGTTATTAAGGTTTATATCATAGATGAGGTTTACATGCTGTCTACAGGGGCTTTTAAATGCCCTCTTAAAG  
ACCTGGAAGAACCAACACAGAATGTAGTCTTTTATTTGGCCACTACTGAATTGCAACAAGATTCTCTCTA  
CTATCTATCCCTGTGCAACGTTTGTAGTTTAAATCAATTAAGACACAGGATATTAAGGAACATATTAC  
TATATCTTAGAATAAAGAAAAATATCAGTTCTGAACCAGAGGCTGTGGAAATCATTGCCAGACGGGCGGAA  
GTTGGAATGGCGGACGCTTGTCTATTTGGATCAAGCCCTGAGTTTGACACAGGGAAATGAGCTGACGA  
CTGCTATCTGGAAGAAATTAAGTGCACCATAGCCTACAGCCTTGGATGATTATGTGGCGGCTTGTCT  
CAACAGGATGTTCCCAAAGCTTTGTCTTGTCTTGAATCTTCTTTTGAACAATGGTAAGAGCATGACTCGTT  
TGTACCGATCTTTTGAATTTTAAAGAGACTTGTAAATTGTTCAAAACAGGGGGGAGAAAATACTCATCAT  
AGTTCACTCTTTGTAGAAAATTTGGCACTTCTCAAAAAAATCTGTTTGAATGATTTCGCTTAGCAACAGT  
GACTTTAGCAGATATTAAGTCTAGTTTGCAGCCCAAGATTTATGCTGAAATGATGACCGTCCGTTTGGCG  
GAAATCAAGTCCGAACAGCTCTATCAGGAGCGGTTGAAATGAAATGCTACGCTGAGACAGGAAATG  
GCCGCTCAAAACAAGAGCTTTCTAATGTAGGTGCGGTTCTTAAACAAGTTGCACAGCTCCTAGTCCAC  
CAGCTACGGGCAAAACAGTCTATCGTGTGATCGCAATAAAGTGCAATCTATCTTACAAGAGGCGCTCGA  
AAATCCTGATTTAGCAGCTCAAAATTTAATTCGTTTGCAGAATGCCTGGGGAGAGGTAATTGAAAGTCTA  
GGTGGGCGGCAAGCTCTGCTCGAGCACCACCACCACCACCACCTGA

2 CFE 82 "homologue of SEQ. ID NO. 78"

ATGTTTCAATTAACCAATAAGTTAGCGGTATCGAACTTGATTAATAAACCAGCAAACTGTACTATCCTTTTGC  
GCTGGCTTTCTTGTGCACTGCTACCTATCTTTTACTCTTAACCTTCAATCCTAAGATTGCGGA  
AATCCGTGGAGGAACAACCATTCAGGCTACACTTGGATTGGTATGTTTGTGCTACCCCTTGGCTGAGC  
ATTATCCTTCTATGCCAATAGTTTGTGATGAAGAACCCTTCAAGGAAGTAGGAATTTATGGCAATGTT  
GGCTTGGAGAAAGCTCATCTTATCAGTATGACCTTAAAGGAGTTAGTGGTATTGGGATTCTAAGTGTG  
GAGCGGCTATCGGATTGGAGCCTTGTGACAAGTTAATTTTCTGCTTCTGCTCAAACTAATGAAATG

2 CFE 82 (contd.)

AAGGTTGAGCTGGTTGCTACCTTCCAGACGAAAGTTGTCATTACAGTGCTTGTGTCTTCGGTTTGATTTT  
 CCTAGGCCTCATGTTCTGAATGCCCTTCGAATCGCCCGTATGAATGCCCTCCAGCTCTCTCGTGAGAAAC  
 CTAGTGGAGAGAAAAAGGTGCTTCCTTCCTCTCCAAACCATTCCTTGGTTCCATAAGTTTATAGGAATTGG  
 CTATTATCTTGGCCCTTACGGTAAAGATCCTCTTACAGCCTTAAACAACCTTCTTCATAGCTGTTTTACTGG  
 TATCTTGGGACTTATCTCTTGTAAATGCAAGGATTACCGTTTCTCCAAATCTTAAAGAAAAATAAGA  
 AATACTATTACCAACCAATAACCTCATATCTGTTCTAACTTGATTTTCCGTATGAAGAAAAATOCAGTI  
 GGACTAGCCACCATCGCTATCTTGTCAACAATGGTTTTGGTAACCATGTTCAGCAGCAGCAAGCATTTTCA  
 ATTCTCAGAAAAGCTTAAAAAAGTTCTAAATCCTCATGATTTTGGGGTTTCAGGGGAAAAATGTTGAAAA  
 AGAAGACTTGGACAACTCTTGAGCCAGTTTGCAAGTGACAAAGGTTATAAGATTAAAGAAAAAGAAAGT  
 ATTCTGTACACTTACTTGTGTTGCGAATCAAGAAGGAACCAAGTTAACTATTTTGAAGAAAGGACAA  
 AACCGTTCCAAACCAAAAAACAGTTTTCATGGTATTTGACCAAAAAAGATTATGAAAAATATGACTGGTCAAA  
 AACTGTCTCTATCAGGAAATGAGGTCCGACTCTTTGCAAGAAATGAGGGAGTTAAAGAACAGAAAGCTC  
 TAACTGTAAATGATCATCAATTTCTGTAAAAGAAGAATTTACTAAAGATTTTATGTCAACCATGTTCCA  
 AATCAGTTAAATATTTGACTGCTGATTACAATTACCTTGTGTACCTGATTACAGCCTTTTGGATCAA  
 TTCCCAATTCGGCTATCTATAATCAGTTTACGGTGGTATGAATGTAATGCCAGTGAAGCAGAAACAA  
 TCAAGGTGCTGAGGAGTATGAAAAATACCTACAAAAGTTAATGCTCAATTAACACTGAAGGTAACATA  
 TGTGTATGGTAGCACTCTAGCAGATGCTAGTCTCAGATGAGTGCCCTCTTTGGTGGTGTCTTCTTTATCG  
 GTATTTCTTATCCATTATCTTTATGGTCCGAACCGTTCTGGTCATCTACTACAAACAAATTTCTGAAGGA  
 TATGAAGACCGTGAAGCGCTTTATTAATCTTGCAGAAAGTCGGTTTAGATCAAAAGCAATCAAGCAAAACCA  
 TCAACAACAGGTTTAACTGTATTCTTCTCTCTTGTCTTCTTGCCTTCTTACATCTAGCCTTTGCTTACC  
 ATATGCTTAGTCTGATTTTAAAGTGATTGGTGTACTGGATACGACTATGATGTTGATTGTGACCTTGTCT  
 ATGTGCTCTATCTTCTCATCGCTATGTGCTGATTTTCATGATTACTTCAAGAAATTATCGCAAGATTGT  
 GCAAAATGCTCGAGCACCACCACCACCACCTGA

Fig 99 (contd.)

2 CFE83 "homologue of SEQ. ID NO. 79"

ATCAAAACAAGATCAACTAAAGGCTTGGCAACCAGCTCAGTTTGACCGTTTGTCCGTATCTTAGAACAAAG  
 ACCAGCTCAATCACGCCTATCTCTTTTCAGGTTTCTTTGGAAGCTTGGAAATGGCGCAATTTTAGCTAAG  
 AGCCTTTTGTGACGGATAAAGTTGGCGTCTTACCATGTGAGAAATGCCGAAGTTGCAAGCTGATTTGAAC  
 AGGAAGAGTTTCCAGATGTCACTTGATTAAGCCAGTCAATCAGGTCTATCAAGACAGAACCGCATTCGGG  
 AATTGGTGGGACAGTTTCTCAAGCAGGGATTGAAAGCCAGCAACAGGTTCTTATCATCGAGCAAGCGG  
 ATAAATGCAATCCCAACGCAGCAATTTCTGCTCAAGGTCTATCGAAGAACCCAGAGTGAAGTTTATAT  
 TTCTTCTGACTAGCOATGAGGAAGAAATGTTACCGCAATCCGAAGTCGGACTCAGATCTTCCACTTT  
 AAAAGCAAGAAGAAAACTTATCTTACTCTTAGAACAAATGGGACTTGTAAAGAAAAAGCGACTCTT  
 TTAGCTAAGTTTAGTCAATCGCGAGCTGAAGCAGAAAAAGTTGGCACATCAGGCAAGTTTGGACCTTGG  
 TCGATGAAGTGAACGCCCTGCTGACTTGGTTAGTAGCTAAGAAAAAGAAAGTTATCTACAGGTTGCCA  
 AATTAGCAACTTGGCAGATGATAAGGAAAAACAGGATCAGGTTTACGGATTCTTGAAGTTCTCTGTGG  
 GCAGGACCTCTTGCAGGTAAGAGTAAGAGTGATTCTACAAGATTTACTAGAAGCTAGAAAAATGTGGCA  
 AGCTAATGTCAGCTTCAAAATGCCATGGAATATCTGGTCTTGAAGAAATACTCGAGCACCACCACCAC  
 CACCACCTGA

Fig 100

2 CFE84 "homologue of SEQ. ID NO. 80"

ATGAATTCATTAAAAATTCTTAAAGAGTGGGATTATTCCTCCTGATTCTGTCTATTACTAGCTTTGAG  
 CCGTATTTTTTTTGGAGAAATGTTCCGCTAGAAAGGACATTCCATGGATCCGACCTAGCGGATGGTGAA  
 ATCTTTTGTGTTAAGCACCTCCCTATGACCGTTTGTATATCGTGGTGGCCCATGAGGAAAGATGGCAA  
 TAAGGAGATCGTCAAGCGCGTGAATTGGAATGCCGTGGCGACACCATTGTTACGAAAAATGATAAACTCTAC  
 ATCAATGACAAAGAAACGGACGAGCCTTATCTAGCAGACTATATCAAACGCTTCAAGGATGACAAAGTTC  
 CAAAGCACTTACTCAGGCAAGGGCTTGAAGGAAATAAAGGAACCTTCTTTAGAAGTATCGCTCAAAAA  
 GCCCAAGCCTTACAGTTGATGTCAACTACAACCAACTTACGTTTACTGTTCCAGAAAGGAGAAATACC  
 TTCTCTCGGAGATGACCGCTTGGTTTCGAGCGGACAGCCGACGTAGGTACCTTCAAAGCAAAAGATAT  
 CACAGGGGAAGCTAAATTCGGCTTCTGGCCAATCACCCGTATCGGAACATTCTCGAGCACCACCACCAC  
 CACCACCTGA

Fig 101

2 CFE85 "homologue of SEQ. ID NO. 81"

ATGGTAGTATTTACAGGTTCAATGTTGAAGAAAGCAATCCAGAAAGGATTGAAAGAAATTAGATATTTCCAA  
 GAATGAAGGCTCATATCAAAGTCAATTTAGGGAGAAAAAAGGCTTTCTTGGTCTATTTGGTAAAAAAC

Fig 102



2 CFE 85 (contd)

Fig 102 (Contd)

AGCCCAAGTGGATATTGAAGCGATTAGTGAAACGACTGTTGTCAAAGCAAATCAACAGGTAGTAAAGG  
CGTTCCGAAAAAATCAATGATTGAAACGAGCGCTGTGAAGACGGTTAGTGAAGAAACCGTTGACCTTGGT  
CATGTGGTTGATGCTATTAATAAATAAGAGGAAGAAGGTCAAGGTATTTCTGATGAAGTCAAGGCTGAA  
ATCTTAAACATGAAGACATGCCAGCACTATCTTAGAAGAACTGGTCACATTGAGATTTTAAATGAAC  
TTCAAATCGAGGAAGCGATGAGGGAAGAAGCAGGCGCTGATGACCTTGAAACTGAGCAAGACCAAGCTG  
AAAGTCAAGAACTAGAAGACTTGGGCTTGAAGTTGAAACGAACTTTGATATTGAACAAGTAGCTACGG  
AAGTAATGGCTTATGTTCAAACGATTATTGATGACATGGATGTTGAGGCTACACTTTCAAATGATTATAA  
CCGTCTAGCATCAATCTACAAATTGACACCAACGAACCAAGGTCGATTATCGGCTACCATGGTAAAGTC  
TTGAAGGCTTGGCACTGTTGGCTCAAATTATCTTTACAACCGCTATTCAGAACCTTCTACGTTACAAT  
CAATGTCATGATTATGTCGAACACCGTGCAGAAGTCTTGCAGACCTATGCGCAAAAATTGGCGACTCGT  
CTTTGCAAGAAGGGCGCAGTCATAAACAGATCCAATGTCAAATAGCGAACGCAAGATTATCCATCGT  
ATTATTTCAGCTATGGATGGCGTGAAGTACTCTGAAGGTGATGAGCCAAATCGCTATGTTGTTGATG  
ATACAAACTGAGCACCACCACCACCACCACTGA

Fig 103

2 CFE 86 "homologue of SEQ. ID NO. 82"

ATGTCAATTTTCCATTATTTAGCAGCGGTAAAGGGGACTCGCATGAAATCTGATTGCCCCAAAGTTT  
GCACAAGGTTGCGGGTATTTCTATGTTGGAACATGTTTCCGTAGTGTGGGAGCTATCCAACCTGAAAAG  
ACAGTAACAGTTGTAGGACACAAAGCAGAATTGGTTGAGGAGGTCTTGGCTGAACAGACAGAATTGTG  
ACTCAATCTGAACAGTTGGGAAGTGGTCATGCAGTTATGATGACAGAGCCTATCTTAGAAGGTTTGTGCA  
GACACACCTTGGTCATTGACGAGATCTCTTAACTCACTGGTGAAGGCTTGAAAACTTGATTGATTT  
CCATATGAATGATAAAAATGTGGCCACTCTTGACTGCTGAAACGGATAATCCTTTGGCTATGGACGA  
ATTGTTGTAATGACAATGCTGAGGTTCTTCGTATTGTTGAGCAGAAGGATGCTACAGATTGTTGAAAAGC  
AAATCAAGGAATCAACACTGGAACATACGTCTTTGACAACGAGCGTTTGTGAGGCTTTGAAAAATAT  
CAATACCAATAACGCTCAAGGCGAATACTATATTACAGACGTCATTGGTATTTCCGTGAAACTGGTGAA  
AAAGTTGGCGTTATACITTTGAAAGATTGTTGATGAAAGTCTTGGGGTAAATGACCGTGTGGCGCTTGGCA  
CAGCTGAGTCAGTTATGCGTCGTCGCATCAATCATAAACACATGGTCAACGGTGTAGCTTTGTCAATCC  
AGAAGCACTTATATCGATATTGATGTTGAGATTGCTCCGGAAGTCAAAATCGAAGCCAATGTTATCTTG  
AAAGGGCAAAACGAAAATTGGTGCTGAGACTGTTTGAACAAACGGTACTTATGTAGTGGACAGCACTATC  
GGAGCAGGAGCGGTCAATTACCAATTCTATGATTGAGGAAAGTAGTGTGACAGACGGTGTGACAGTCCGT  
CCTTATGCTCACAATCGTCCAAATTCAAGTGTGGGTGCCAAGTTCATATTGGTAACTTTGTTGAGGTGAA  
AGGATCTTCAATCCGTGAGAAATACCAAGGCTGGTCAATTGACTTATATCGGAACTGTGAAGTGGGAAGC  
AAGCTTAATTTGGGTGCTGGAACATATTACAGTCAACTATGACCGCAAAAACAAATACAAGACAGTCAATG  
GAGACAATGTCTTTGTTGGTTCAAATTCAACCATTATTGACCAAGTAGAACTTGGTGACAATCCCTCGTT  
GTTCTGTTGTAOACTATTACTAAAGACGTGCCAGCAGATGCTATTGCTATTGGTCCGGGTCTCAOATCA  
ATAAAGACGAATATGCAACACGTCTTCTCATCATCTAAGAACCAGCTCGAGCACCACCACCACCACCA  
CTGA

Fig 104

2 CFE 87 "homologue of SEQ. ID NO. 83"

ATGTCCAAGATTCTAGTATTGTTGTCACCAAAATCCAGACTCAGATGCCATCGGGTCACTGTAGCTTTTGC  
CTACCTTCAAAAGAAAGCTTACGGTTTGGATACGGAAGCTGTTGCCCTTGGAACTCCAAATGAAGAAACA  
GCCTTTGCTTGAACATTTTGGTGTGGAAGCACCACGTGTTATCACTTCTGCCAAAGCAGAGGGGGCAG  
AGCAAGTATCTTGACTGACCACAATGAATTCCAACAATCTGTATCAGATATCGCTGAAGTAGAAGTTTA  
CGCTGTTGTAGACCACCACCGTGTGGCTAACTTTGAACTGCAAGCCCACTTTACATGCGTTTGGAGCCA  
GTTGGATCAGCGTCTTCAATCGTTTACCGTATGTTCAAAGAATATGGTGTAGCTGTGCCTAAAGAGATTG  
CAGGTTTATGCTTTTCAAGTTTGATTTCAGATACCTTCTTTTGAATCACCACCAACACACCCCAACAGAT  
AAAATCATGCTCTCTGAATTGGCTGAATTGGCTGTTGTAACCTTGAAGAATATGGTTTGGCAATGTTGA  
AAGCTGTACCAACTTGGCTAGCAAAATCTGCTGAAGAATGATTGACATCGATGCTAAGACTTTGAACT  
CAACGGAAATAATGTCCGTGTTGCCCAAGTGAACACAGTTGACATCGCTGAAGTTTGGAAACGCCAAGCA  
GAAATTGAAGCTGCAATGCAAGCTGCCAAGCAATCAAACGGTACTCTGACTTTGTCTTGATGATTACAG  
ATACTGTCAACTCAAACCTCAGAAATATTGGCTCTTGGTGCCAAATATGGACAAGGTGCAAGCGGCTTCAA  
TTTCAAACCTTGAAAAAATCATGCTTCTTGGTGGTGGCTTTCACGTAAGAAACAAGTGTACCTCAAT  
TAAGTGAAGCTTTAATACGCTCGAGCACCACCACCACCACCACTGA

Fig 105

2 CFE 88 "homologue of SEQ. ID NO. 84"

ATGATTTCAAAGAGATTAGAATTGGTAGCTTCTTTGTGTACAGGGGGCTATTTTACTAGATGTGGAA  
GTGACCAATGCTTATCTGCCTATCGAGTTGGTTGAGAGAGGCCAAATCAAAAGCGCTATTGCAGGTGAGGT

2CFE 88 (contd)

GOTGGAAGGTCCCTATCAGTCTCGGTTAAAAATGTTGAGGCTCACGGCCTAAAGGAGAAAAATCCAAGT  
 CCGTTTATGCCAATGGCTTGGCAGCTTTTGAAGAGACTGACCAAGTGTCTGTCATTACCATTGCTGGCATG  
 GGTGGTGGTTTATTGCTAGGATTTTGAAGAAGGTTTGGGGAAGTTAGCTAATGTAGAGCGTTTGATCC  
 TCGAGCCCAATAATCGTGAAGACGACTTGGCTATCTGGCTACAGGATCATGGATTCCAGATTGTAGCAGA  
 AAGAATCTTAGAAGAAGCTGGAAAGTTTATGAGATTTGGTGGTGOAAGCAGGACAAATGAAOCTATC  
 AGCCAGTGATGTTGGCTTTGGTCCCTTCTGTCCAAAGAAAGTCAGTCCAGTATTTGTCCAAAAATGGCAA  
 AAAGAAGCTGAGAAGCTAGAGTTCCGCCCTCGACAAATCCCAGAAAAAATCTGGAAGAACGTCAAGTT  
 CTAGTAGATAAGATTCAAGCTATCAAGGAGGTGCTCCATGTTAGCAAGCTCGAGCACCACCACCACC  
 ACTGA

## 2 CFE89 "homologue of SEQ. ID NO. 85"

ATGAATTAAGCGATATTAAGACTTGATGACTCAATTTGACCAGTCAAGTTTGAGAGAATTTCTTATA  
 AAAATGGGACCGATGAGTTGCCAGTTTAGCAAGAAATGAAGCAAGACCTGTGCTGAAGTTGCAACTCAAG  
 TCGCTCCAGCAACCGTTCTAGCAACACCGAGTCCAGTAGCTCTACATCTGCTCCAGCAGAGACTGTAGC  
 AGAAGAAGTTCCAGCTCCAGCTGAAGCAAGTGTGGCTACTGAGGGAAATCTTGTAGAGAGTCCACTTGT  
 GGAGTGGTTTACTTGGCTGGCTGGACAGATAAAACCTGCCTTCGTTACAGTTGGTGATAGTGTCAAAAAAG  
 GTCAAAATTTGGTAATTATCGAAGCCATGAAAGTCATGAATGAAATCCAGCTCCTAAGGATGGTGTGT  
 AACGGAATTTCTGCTCTAACGAAGAAATGGTTGAGTTTGGTAAAGGATTGGTACGTATCAAACTCGAG  
 AACCAACCAACCACTGA

## 2 CFE90 "homologue of SEQ. ID NO. 86"

ATCAAACTAAATCGAGTAGTGTAACAGGTTATGGAGTAACATCTCCAATCGGAAATACACCAGAAGAA  
 TTTTGGAAATAGTTTAGCAACTGGGAAAAATCGGCATTGGTGGCATTACAAAAATTTGATCATAGTGACTTTG  
 ATCTGCATAATGCGGCAGAAATCCAAGATTTTCCGTTTCGATAAATACTTTGTAAAAAAGATACCAACCG  
 TTTTGATAACTATTCTTTATATGCTTGTATGCAGCCCAAGAGGCTGTAAACCATGCCAATCTTGATGTAG  
 AGCTCTTAATAGGGATCGTTTGGTGTTATCGTTGCATCTGGTATTGGTGGAAATCAAGGAAATTTGAAGA  
 TCAGGTACTTGCCTTCATGAAAAAGGACCCAAACGTGTCAAACCAATGACTCTTCCAAAAGCTTTACCA  
 AATATGGCTTCTGGGAATGTAGCCATGCGTTTGGTGCAAACGGTGTGTGTAATCTATCAATACTGCCTG  
 CTCTTCATCAAAATGATGCGATTGGGGATGCTTCCGCTCCATTAAAGTTTGGTTTCCAAAGATGTGATGTTGG  
 TGGGAGGAACAGAAGCTTCTATCACACCTTTTCCCATCGCTGGTTTCCAAAGCCTTAACAGCTCTCTCTACT  
 ACAGAGGATCCAACTCGTGCTTCGATCCCATTTTGATAAGGATCGCAATGGGTTTGTATGGGTGAAGGTT  
 CACGGAATGTTGTTGTAGAAAAGTCTTGAACACGCTGAAAAACGTGGAGCTACTATCCTGGCTGAAGTGGT  
 TGGTTACGGAAATACTTGTGATGCTTACCACATGACTTCTCCACATCCAGAAGGTGAGGGAGCTATCAAG  
 GGCATCAAACTAGCCTTGGAAAGAAOCTGAGATTCTCCAGAGCAAGTAGCCTATGTTAATGCTCACGGAA  
 CGTCAACTCCTGCCAATGAAAAAGGAGAAAGTGGTGCTATCGTAGCTGTCTTGGTAAGGAAAGTACCTGT  
 ATCATCAACCAAGTCTTTTACAGGACATTTGCTGGGGGCTGCGGCTGACAGTAGAAGCTATCGTACCACATC  
 GAAAGTATGCGTCATAACTTTGTACCAATGACAGCTGGGACAAGTGAAGTATCAGATTATCGAAGCTA  
 ATGTCGTTTATGGACAAGGTTTGGAGAAAGAAATTCATACGCTATTTCAAATACTTTGGTTTTGGAGGC  
 CAAATGCAAGTTCTTGTCTTCAACGTTGGGAGAATAGACTCGAGCACCACCACCACCACCCTGA

## 2 CFE91 "homologue of SEQ. ID NO. 87"

ATGAACATCTATGATCAACTACAAGCTGTAGAAGACCGTTATGAAGAAGTAGGAGAATTGCTGAGTGAC  
 CCTGATGTCGTTTCAGACACCAAGCGTTTATGAGGCTTCAAAAAGAAAGCTTCCAATCGTGACACCG  
 TAATAGCTACCGTGAGTATAAACAAGTCTTCAAAATATCGTCGATGCCGAAGAGATGATTAAGGAATC  
 AGCCGGAGATGCGGACTTGAAGAAATGGCCAAGCAAGAACTCAAAGATGCCAAGGCTGAAAAAGAAAG  
 AATATGAAGAAAACTGAAAAATTTGCTCCTTCCAAAGGATCCAAACGATGACAAGAAATATCATCTTGA  
 AATCCGTGGAGCAGCTGGTGGAGACGAAGCGGCACTTTTCGCTGGAGATTGCTAACTATGTACCAAAAG  
 TATCCGGAAGGCCAAGGTTGGCGCTTTGAAGTCATGGAAGCCTCTATGAATGGTGTGCGTGGTTTTAAAG  
 AAGTGGTTGCTATGGTTTCAOGTCACTGTGTATACTTAAGCTTAAGTATGAATCAGGTGCCACCGTGTG  
 CAACGTGTTCTGTGACAGAAAGCCAAGGCCGTGTTCACTTCCAGACGACAGTTCTTGTATGCCAG  
 AAGTTGAAGAGGTTGAATACGACATTGATCCAAAAGACCTTCGTGTGACATCTATCACGCCCTCTGGTGC  
 TGGTGGACAGAAAGTCAATAAGGTTGCGACTGCCGTTGCTATCGTTCACTTGCCAACCATAATCAAGGTT  
 GAGATGCAAGGAAGCAAGCTACCEAGCAGAAGAACCCGAGAGGCTATGAAGATTATCCGTGCACGCGTC  
 GCTGACCACTTTGCTCAGATTGCTCAGGATGAACAAGACGCTGAGCGTAAGTCGACAATCGGTACTGGTG  
 ACCGTTCAAGACGGATCCGAACCTTATAACTCCCAAAAACCGTGTACAGACCACCGTATCGGCTTGAC

(contd.)

Fig 108

2 CFE 91 (contd.)

CGTCCAAAACTAGATACGATTTTGTCTGGTAAATTGGACGAAGTTGTGGATGCCTTGGTGCTTTATGACC  
AAACACAAAACTAGAAGAATTAAACAAACTCGAGCACCACCACCACCACCTGA

## 2 CFE92, "homologue of SEq. ID NO. 88"

ATGGCCTACACTCTTAAACCTGAAGAAAGTCGGCGTTTTTGCCATCGGTGGTCTAGGAGAAATCGGGAAAA  
ACACTACCGAATTGAATACCAAGACGAGATTATCATCGTCGATGCTGGGATTAAATTCACAGAAATGATGA  
CTTGGCTGGTATCGACTATGTCATTCTGACTACTCTTACATCGTAGACAATATCGACCGGTCAAGGCTG  
TTTAAATCACACACGGACACGAGGACCACATTGGTGGGATTCCGTTCTACTCAAGCAAGCAAATGTCCC  
TATTTATGCTGGACCGCTTGCCTTGGCTTTGATCCGTGGGAAACTCGAAGAACACGGCCTCTTGGCAAC  
QCCAACTTTACGAAATCAACCACAACACCGAGTTGACCTTTAAAAATCTCAAGGCAACTTTCTTTAGAA  
CGACTACTCTATTCCAGAGCCTTTGGGGATTGTCATTCTACTCTCAAGGAAAAATCGTCTGTACGGGT  
GACTTTAAGTTCGACTTTACTCCAGTTGGAGAACCTGCGGACTTGCATCGTATGGCTGCGCTTGGTGAAG  
AAGGCGTGTCTGTCTCTGTCTGACTCGACAAATGCGGAAGTACCAACCTTTACCAACTCTGAAAAAGT  
CGTTGGTCAGTCCATTATGAAGATTATCCAAGGTATTGAAGGACGTATCATCTTTGCATCCTTTGGCTCAA  
ATATCTTCCGTCTCCAGCAGGCAACAGAAGCTGCTTTAAGACTGGACGCAAGATTGGGTCTTTGGTCC  
TTCTATGAAAAGGCCATTGTCAACGGAATCGATCTTGGCTACATCAAGGCTCCTAAGGGAACCTTTATC  
QAQCCAAATGAAATCAAAGATTATCCTGCAGGAGAAGTTCTTATCCTCTGTACAGGTAGTCAGGGTGAGC  
CTATGCGAGCCTCTCTCGTATCGCCAACGGAACCCACCGTCAAGTACAATTACAACCAAGGTGATACCGT  
TATCTTCTCTTCTAGTCCCATCCCTGGAAACACTACTAGCGTCAACAAGCTGATTAAACATCAITTTCTGAAG  
CTGCTGTCGAAAGTTATCCACGGTAAAGTGAACAATATCCCATACATCTGGACACGGTGCCAGCAAGAGC  
AAAAATCATGCTCCGCTTGATTAAAGCCAAATACTTCAATGCGCTGTCCACGGTGAATACCGCATGCAAAA  
AGTCCACGCTGGACTAGCAGTGGATCTGGTGTGTGGAAGGACAATATCTTTATCATGAGCAATGGCGAT  
GTCTTCCCTTACTGCTGACTCAGCTCGTATCGCAGGTCAITTTCAACGCCCAAGATATCTATGTCGATGG  
AAATCGTATCGGTGAAAATTGGCGCAGCTGTCTCAAGATCGTCCGATCTATCTGAAGACGGTGTCTCT  
CTAGCAGTCGCAACTGTTGACTTCAAAATCGCAGATGATTCTGTCTGGGCCAGATATCTCAGCCGAGGCT  
TTGCTCATAGAGAGTCTGGAGACTTGATTGCGCAAAGCCAGCGTATCTCTTCAATGCCATTCTGATC  
GCACTGAAAAATAAGGATGCTAGCGTGCAATCTGTCAA  
TCTATGAAAATACCGAACGTGAACCGATCATCATCCCG/  
CCACCACCACCACCCTGA

Fig 109

## 2 CFE94

ATGGCTACGGCAACAAAAAGAAAAATCAACAGTTA/  
AAGGCCAAGACGATTGAAAAATATCTAGGCAGAACTACAAGGTTTTAGCCAGTGTGCGGCATATCCGT  
GATTTGAAGAAATCCAGTATGTCCGTGATATTGAAAAATTAATGAACCGCAATATATTAATATCCGAG  
GAAAAGCCCTCTTATCAATGACTTGAAAAAGAAAGCTAAAAAAGCTAATAAAGTTTTCTCCGCGAGT  
ACCCGACCGTGAAGGAGAAGCGATTTCTTGGCATTGGCCCATATTTCTCAACTTGGATGAAAATGATGC  
CAACCGTGTGCTTCAATGAAATCACCAAGGATGCAATCAAAAATGCTTTAAAGAACCTCGTAAGATC  
GATATGCACTTGGTGGATGCCCAACAAGCTCGTCGGATCTTGGATCGCTTGGTAGGGTATTGATTTCCG  
CTATTTTGTGGAGAAGGTCAAGAAGGGCTTGTACGAGGTGCGGTTCAGTCCATTGCCCTTAACTCAT  
CATTGACCGTGAAAAATGAAATCAATGCCCTTCCAGCCAGAAAGAACTGACAGTGTGATGCTGTCTTAAA  
AAGGGAACCAACAATTTCATGCTTCTCTATGAGTATGATGGTAAAAAGATGAAACTGACCAAGCAAT  
AAGGAAGTCAAGGAAGTCTTGTCTCGTCTGACGATGAAAGACTTTTCAATAGATCAGGTGGATAAGAAA  
GACCGTAAGCGCAATGCTCTTTACCTATACCACTTCATCTATGCAGATGGATGCTGCCAATAAAATCA  
ATTCCGTACTCGAAAAACCATGATGGTTGCCCAACAGCTCTATGAAGGAATTAATATCGGTCTGGTGT  
TCAAGGTTTGATTACCTATATGCGTACCGATTGACTCGTATCAGTCTGTAGCGCAAAATGAGGCGGCA  
AGCTTCATTACGATCGTTTTGGTAGCAAGTATTCTAAGCACGGTAGCAAGGTCAAAAACGCATCAGGTG  
CTCAGGATGCCATGAGGCTATTGCTCCGTCAAGTGTCTTTAATACACCAGAAAGCATCGCTAAGTATCT  
GGACAAGGATCAGCTCAAGCTATATACCTTATCTGGAATCGTTTTGTGGCTAGCCAGATGACAGCGGCC  
GTTTTGATACCATGGCTOTTAATTTGTCTCAAAAAGGGTTCAATTTGCTGCCAATGGTAGTCAGGTTAA  
GTTGATGGTATCTTGGCATTATATGATCTGACAAGAATAAGATGTTACCGGACATGGTTGTGGAG  
ATGTGGTCAAAACAGGTCAAATAGCAAAACAGCAACATTTCAACCAACCGCTGCCCGTTATTCTGAAGC  
AACACTGATTAACCTTAGAGGAAAAATGGGGTTGGACGTCCATCAAGCTACGCGCCCAACCATGAAAC  
CATTCAGAAAGCTTATTATGTTGCGCTGGCAGCCAAACGTTTTGAACCAACAGAGTTGGGAGAAATTTG  
AATAAGCTCATGTTGAATATTTCCAGATATCGTAAACGTGACCTTCACAGCTGAAATGGAAGTAAAC  
TGGATGATGTCGAAGTCGGAAGAGCAGTGGCGACGGGTCAATTGATGCTTTTACAAACCATCTCTAA

Fig 110

JCFE 94 (contd)

Fig 110 (contd)

ACAAGTTGCCAAGGCTGAAGAAGAAATGGAAAAATCCAGATTAAGGATGAACCAGCTGGATTGACTG  
TGAAGTGTGTGTAGTCCAATGGTCATTAACCTTGGTCGTTTGGTAAATCTACGCTTGTAGCAATTTC  
CAGATTGCCATCATACCAAGCAATCGTGAAGAGAGATTGGTGTGAGTGTCCAAGCTGTATCAGGGACA  
AATTATTGAGCGAAAAACCAAGCGTAATCGCCTATTCTATGGTTGCAATCGCTATCCAGAATGTGAATTT  
ACCTCTTGGGACAAGCCTGTTGGTCTGACTGTCCAAAATGTGGCAACTTCCACATGGAGAAAAAGTCC  
GTGCTGTGGCAAGCAGGTTGTTGTAGCAAAAGGCGACTACGAGGAAGAAAAAGATGGCTCTTTGTCAACT  
GCTCGAGCACACCACCACCACCACTGA

## 2 CFE95 "homologue of SEQ. ID NO. 91"

Fig 111

ATCTTTATTTCCATCAGTGTGGAATTGTGACATTTTACTAAGTTAGTAGGAATTCGGCCTTTATCCA  
ATTTTATAGAAAGCGCAAAATTACAGGCCAGCAGATGCATGAGGATGTCAAACAGCATCAGGCAAAAGC  
TGGGACTCCTACAATGGGAGCTTTGGTTTCTTGATTCTCTGTTTGGTTGCTTTCTTTTCGCCCTATT  
AGTAGCAATTCAGCAATAATGTGGGAATGATTTTGTTCATCTTGGTCTTGTATGGCTTGGTCTGGATTTT  
AGATGACTTTCTCAAGGTCTTTCTGTAATAATGAGGGGCTAATCCTAAGCAAAAATTAGCTCTTCAO  
CTTCTAGGTGGAGTTATCTTCTATCTTTCTATGAGCGCGGTGGCGATATCTGTCTGTCTTTGTTATCCA  
GTTCTATTGGGATTTTCTATATTTCTTCGCTCTTTCTGGCTAGTCGGTTTTCAAAACGCAAGTAACTTG  
ACAGAAGGTGTGACGGTTTAGCTAGTATTTCCGTTGTGATTAGTTTGTTCCTATGGAGTTATTGCCTA  
TGTGCAAGGTGAGATGATATTTCTTAGTGATTCTTGCCATGATTGGTGGTTTGTCTGGTTTCTTCATCTT  
TAACCAATAAGCTGCAAGGTCTTTATGGGTGATGTGGGAAAGTTTGGCCCTAGGTGGGATGCTGGCAGCT  
ATCTCTATGGCTCTCCACCAGGAATGGACTCTCTTGATTATCGGAATTGTGTATGTTTTGAAACAACCTTC  
TGTTATGATGCAAGTCAGTTATTTCAAAGTACAGGTGATGTAACGATTTTCCGTATGACGCTGTACATC  
ACCAATTGAGCTTGGGGGATTGTCTGGTAAAGGAAATCCTTGACGAGTGGAAAGGTGACTTCTTCTT  
TTGGGGAGTTGCTTCTAGCAAGTCTCTGACCCTAGCAATTTTATATTGATGCTCGAGCACCACCACC  
ACCACCCTGA

## 2 CFE96 "homologue of SEQ. ID NO. 92"

Fig 112

ATGGCAAGCGAATTTTCACTTGAAAAAACTCGTAATATCGGTATCATGGCTCAGCTCGATGCCGGTAAAA  
CAACAATACTAGAGCGTATTCTTTACTACACTGGTAAAAATCCACAAAATCGGTGAAACTCAGGAAGGTGC  
GTCACAAATGGACTGATGGAGCAAGAGCAAGAACGTGGTATCAGATCACATCTGCTGCCACAACAGC  
TCAATGGAACAACCAAGCGGTAAACATCATCGACACACCAGGACAGCTGGACTTCACAATCGAAGTACA  
ACGTTCTCTCGTGTATTGGATGGTGGGTTACCGTTCTTGACTCACAATCAGGTGTTGAGCCTCAAACTG  
AAACAGTTTGGCGTCAAGCAACTGAGTACGGAGTTCCACGATCGTATTGTCACAAAATGGACAAAAT  
CGGTGCTGACTTCTTTACTCTGTAAGCACACTTCACGATCGTCTTCAAGCAAAATGCACACCCAATCCAAT  
TCCCAATCGGTTCTGAAGATGACTTCCGTGGTATCATTGACTTGATCAAGATGAAAGCTGAAATCTATAC  
TAACGAAGCTTGGTACGGATATCCTTGAAGAGACATCCCAGCTGAATACCTTGACCAAGCTCAAGAAATAC  
CGTGAAGAAATTOATTGAAGCAGTTGCTGAAACTGACGAAGAATTGATGATGAAATACCTCGAAGGTGAA  
GAAATCACTAAACGAAGAATTGAAAGCTGGTATCCGTAAAGCGACTATCAACGTTGAATTTCTCCAGTAT  
TGTGTGTTTACGCCCTTCAAAAAACAAAGGTGTTCAATTGATGCTTGTATGCGGTTATCGACTACCTTCAAAGT  
CCAATTGACATCCCAOCAAATCAAAGGTATTAACCCAGATACAGACGCTGAAGAAAATTCGTCCAGCATCTG  
ACCAAGAGCCATTGTCAGCTCTTGCCCTTCAAGATCATGACTGACCCATTCTGATGGTCTGTTGACATTCTTC  
CGTGTTTACTCAGGTGTTTCTCAATCAGGTTTACATCGTATTGAAATCTTCTAAAGGTAAACGTGAACGAT  
CCGACGTATCCTTCAAATGCAAGCTAACAGCCGTCAAGAAATCGACACTGTTTACTCAGGTGATATCGCT  
GCTGGCGTTGGTTTGAAGATATACTACAACCTGGTGAATTCATTGACAGATGAAAAAGCTAAAAATCATCCTTG  
AGTCAATCAAGTTCCAGAACCAGTTATCCAATTGATGGTTGAGCCAAAATCTAAAGCTGACCAAGACAA  
GATGGGTATCGCCCTTCAAAAAATGGCTGAAGAAGATCCAACATTCGCGGTTGAAACAAACGTTGAAAGT  
GCTGAAACAGTTATCTCAGGTATGGGTGAACTTCACCTTGACGCTCCTTGTGATCGTATGCGTCTGAGTT  
CAAAGTTGAAGCGAAGCTAGGTGCTCCTCAAGTATCTTACCGTGAAACATTCCGCGCTTCTACTCAAGCA  
CGGGAATCTTCAAACGTCAGTCTGGTGGTAAAGGTCAAATTCGGTGAATGATGGAATTGAATTTACTCCAA  
ACGAAGAAGGTAAAGGATTGCAATTCGAAAAACGCAATCGTCCGTGGTGTGGTTTCTCGTGAATTTATCCC  
ACCGGTTGAAAGGTTTGGTGAATCTATGGCTAACGGTGTCTTGCAGGTTACCCAATGGTTGACGTT  
AAAGCTAAGCTTTATGATGGTTTATATACGATGTGCACTCATCTGAAACTGCCCTCAAGATTGCGGCTTC  
ACTTCCCTTAAAGAGCTGCTAAATCAGCACAAACCAGCTATCCTTGAACCAATGATGCTTGAACAAATC  
ACTGTTCCAGAAAGAAAACCTTGGTGAATGTTATGGGTACGTAACCTGCTCGTGGACGTTGATGATGTA  
TGAAGCACACGTTAACAGCAAAATCGTCTGTTTACGTTCCACTTGTGAAATGTTCCGTTACGCAAC  
AGTCTTCTGTTCTGCAATCTCAAGGACGTGGTACATTGATGGTATTGACCACTACGAAGATGTACCTA

(Cont'd)

Fig 112

2CFE 96 (cont'd)

AGTCAGTACAAGAGAAATTATTAAAGAAAAATAAAGGTGAAGACCTCGAGCACCACCACCACCACCTG

2CFE97 "homologue of SEQ. ID NO. 93"

ATGCCAAATTAACATATTCCATTTTCACCGCTGATATCAGAGAAGCAGAAATTGCTGAAGTAGCGGATA  
CCCTGCGTTCTGGTTGGATCACAACAGGTCCATAAACAAAAGAACTGGAGCGCCGCTTGCTCTTTACAC  
ACAGACACCTAAGACTGTTGTCTCAACTCTGCGACAGCCGCTCTGGAGTTGATTTTACGCGTTTGGAAO  
TGGGAOCTGGTGATGAAGTCATCGTTCCAGCCATGACCTATACGGCTTCATGTAGTGTCTATTACGCACGT  
GGGAGCAACCCCTGTCATGGTGGATATCCAAGCAGATACGTTTGAGATGGACTATGACCTGCTTGAGCAA  
GCTATCACTGAAGAACTAAGGTGATTATCCAGTAGAGCTCGCAGGGATTGTTTGGCATTATGACCGTT  
TGTTCCAGTGGTGGAGAAAAACGTGACTTCTTTACCGCTTCAAGCAAGTGCCAAAAAGCCCTTTAACCG  
TATTGTCATTGTCTCTGATAGTGGCCACGCTTTGGGATCTACTTATAAAGGAGAACCTTCTGGTTCTATCG  
CTCAATTTACTTCTCTCTCATTCATGCTGTTAAGAACTTTACAACGGCAGAAAGGTGGAAOTGCGACTTGG  
AAAGCCAAATCCAGTGAATTGATGACGAAGAGATGTACAAGGAATTCCAAATCCTTTCCCTTCACGGGCAAA  
CTAAGGATGCTCTTGGCAAGATGCAACTGGGGTCTAGGGAATACGATATCGTTACACCCAGCCTATAAGTG  
CAACATGACCGATATCATGGCTTCACTTGGTTTGGTACAATTGGACCGCTATCCAAGTTTGTGCAACGCC  
GTAAAGACATTTGGTGAACCGCTATGATAGTGGTTTTCAGGTTCTCGCATCCATCCTTTGGCAGACAAAGAC  
TGAAACTGTGCAATCTTCACGCCACCTCTACATCACCCTGTGTAAGGAGTAAGECTAGAAAGAACGCAAC  
CTCATCTCCAAGAATTGGCTAAAGCAGGAATTGCAAGTAATGTTCACTACAAACCGCTTCTCTCTTGA  
CAGCCTATAAGAATCTTGGATTGATATGACGAACATCTCTAAGGCCTATGCCTTCTTGAAGATGAATTT  
ADCTCCTCTTTCATACTAAATTAAGCGATGAAGAGTAAGACTATATCATTGAGACTTTCAAAACAGTTT  
CTGAAAAAGTCTAATCTTTATCAAAAAAATCTCGAGCACCACCACCACCACCTG

Fig 113

2CFE99 "homologue of SEQ. ID NO. 95"

ATGTTTATACITATTITGCGTGGATTAGTTGATTGCTCTTATGGTCCATCAATGGCAATGCTCACTATCAT  
AATACTGATAAAATTCCTAATCAAGATGAAAATTATATTTAGTTGCGCTCACCGTACCTGGTGGGATC  
CTGTTTATATGGCCTTTGGACCAAGCCAAAACAGTTTCATCTTATGGCAAAAAAAGAACTCTTACCAA  
CCGATCTTTGTTGGTGGATTCGTATGTGTGGCGCTTTCCTATCOACCGTGAAGAAATCCACGCGCCTCAG  
CCATCAAAATCTCTATCAACGTTCTCAAAAAAAGTGACCGCTCTCTCATCATGTTTCCAAGTGGTAGCCGC  
CACTCAACAGATGTCAAGGGGGGGCGCAGCACTGATTGGCAAAATGGCCAAAGTCCGTATCATGCGGTT  
ACCTACACCGGTCCCATGACTTTGAAGGGCTTGATTAGCGGTGAACGTGTGATATGAACCTTTGGAAATC  
CAATCGATATCTCAGATATCAAGAAAATGAATGATGAAGGCATTGAAACAGTGGCAATCGTATTCAAA  
CAGAAATCCAACGTCTGGACGAAGAAACGAACCAATGGCACAATGATAAAAAACCAATTECACTCTGGT  
GTTTATCCGCTACCTGCCCCATCTTGTCTATTATCTCGCTATCCTAACCATCATCTTTAGCTTTATCG  
CAAGCTTCATCTGGAACCCAGATAAGAAAAGAGAACTTGCCTCGAGCACCACCACCACCACCT  
GA

Fig 114

2CFE101 "homologue of SEQ. ID NO. 97"

ATCACCACCGAATTTTACATTTTGAAAAAATCAGCCGCGAGACTTGGCAATCTTTACATCGAAAGACAA  
CACCTCCTTTGACAGAAGAAGAAATTGGAATCTATCAAGAGTTTAAAGACCAATCAGTCTCCAAGACGT  
TACAGATATCTATCTCCCTTGGCTCATCTGATTGAGATTACAGCGAACTAAGGAAGATTTAGCCTTTT  
CAAAAGGAATTTTCTCCAACGTGAAAGTAAATCTCAACCTTTTATTATGGGGTTTCTGGGAGTGTGGC  
GTTGGAAATTCACAACCAAGTGGCTACTTCAAAATCTCTACTGTCCCGTACGTTTACAGATGCTACGGTTG  
AGTTGGTTACAACCTGATGGTTTCTCTATCCCAATCAAACTTGAATTGAGCAGGGGATTTTAAATCGTAAA  
GGATTCTGAAAGCTATGATATGGAAGCTCTTCTCAACTTCTTGGACCGCATCAAAAATGGACAAGATG  
TAGATATTCCTGTCTATCTCATGAAGTTTACGACATCGTACCCGAAGAGAAAACAAAGTGTCAAAGCTGC  
TGATTTTGAATTTGTTGAGGGAATCAATGCTTTTCAAAATCCACAAAACGATCGTCTCTATATCACTGACT  
TCTTTGACTTTTCCATCTATGTAGATGCTGGAGTGGATGATATTGAAAGTTGGTATCTGGACCGTTTCTTG  
AAAATGGTGAAGTCTAGCCCAAAACGACCTGATAGCTACTATTATCGTTTACTCAGATGCCGATTGGGG  
AAGTGGAAAGCCTTGGCCATCAGGTCTGGACCAATCAATCTCACAATCTACAAAATTTATTTGAACC  
AACCAAGAAATCTGACGAAGTGATTCTTCATAAAGCAAGAACCATGAATCGATGAAATTTACTTAAA  
AAAGCTGAGGACCAACCAACCAACCACTGA

Fig 115

2CFE102 "homologue of SEQ. ID NO. 98"

ATGGAAATTTTATTATTAACAGATGTTGGTCAGAAACGAACAAATAACCAAGACTATGTCAACCACTATG  
TCAATAGAGCTGGACGTACCATGATTATTTAGCTGATGGGATGGGAGGTATCGCGCAGGGAATATCGC

Fig 116

2 CFE 102 (contd)

Fig 116 (contd)

TAGTGAATGGCGGTACAGACCTGGGTGTAGCTTGGGTTGATACCCAGATCGATACAGTCAATGAAGTG  
 OGTGAATGGTTGCGCCATTACCTAGAAATTGAAATCAAAAGATTACCCAGCTTGGTCAGGATGAAGCTT  
 ACAGAGGCATGGGAACCTACTTTGGAAGTCCTTGTATTATGATAATCAGGCTATCTATGCTCATATTGGT  
 GATTCCCGTATCGGCTTGATTCTGGGAGAAGAATACCATCAGTTGACGAGCGATCAATTCCTTGGTTAAATG  
 AATTGCTCAAGGCTGGTCAATTGACACCAGAAGAGGCAGAAGCTCATCCGCAAAAAAATATTATCACCC  
 AGTCTATTGGGCAAAAAGATGAAATTCAGCCTGATTTTGGGACAGTTATCCTTGAGTCAGGTGACTATCT  
 CTTCCTCAATAGTGACGGCTTGACCAACATGATTTCAGGCAGTGAGATTCTGTATATTGTAACCACTGAT  
 ATTCTTTAGCAGATAAAACGGAGACACTTGTTCGTTTGTCTAACAAATGCAGGAGGTTTAGACAACATTA  
 CGTTGCCCTTGTTCCTATGAACGAGGAGGATGAAGAACTCGAGCACCACCACCACCACCTGA

Fig 117

## 2 CFE103 "homologue of SEQ. ID NO. 99"

ATGACGATACAGATGAAGAATACAGGTAAACGAATTGATCTGATAGCCAATAGAAAACCGCAGAGTCAA  
 AGGGTTTGTATGAATTGCGAGATCGTTTGAAGAGAAATCAGTTTATACTCAATGATACCAATCCGGATA  
 TTCTCATTTCCATTGGCGGGGATGGTATGCTCTTGTCCGCCCTTCATAAGTACGAAAATCAGCTTGACAAAG  
 GTCCGCTTATCGGCTTCATACTGGACATTGGGCTTCTATACAGATTATCGTGATTTTGAGTTGGACAA  
 GCTAGTGACTAATTTGCAACTAGATACTGGGGCAAGGGTTTCTTACCCTGTTCTGAATGTGAAGTCTTTT  
 TTCAAAATGGTGAAGTTAAGATTTTCAGAGCACTCAACGAAGCCAGCATCCGAGGTCTGATCGAACCAT  
 GBTGGCAATATTGTAATAAATGGTGTTCCTTTGAACGTTTTCGTGGAGACGGGCTAACAGTTTTCOACA  
 CCGACTGGTAGTACTGCCATAACAAAGTCTCTTGGCGGTGCTGTTTACACCCTACCATTGAAGCTTTGCA  
 ATTAACGGAGATTGCCAGCCTTAATAATCGTGTCTATCGAACATTGGGCTCTTCCATTATTGTGCTTAAGA  
 AGATAAGATTGAACCTTATCCAAACAAGAAACGATTATCATACTATTTCGGTTGACAAATAGCCTTATTCT  
 TTCCGTAATATTGAGCGTATTGAGTATCAAATCGACCTATCAAGATTCACTTTGTGCGGACCTTAGCCA  
 TACCAGTTCTGGAACCGTGTAAAGGATGCCTTTATCGGTGAGGTGGATGAACTCGAGCACCACCACCAC  
 CACCACTGA

Fig 118

## 2 CFE104 "homologue of SEQ. ID NO. 100"

ATGTCAAAAGAAATTAATTTTCATCAGATGCCCGTTCAGCCATGTTTCGTGGTGTGCATATCCTTGCA  
 ACCTGTAAAGTAACCTTGGGACCAAAAGGTGCAATGTCGTTCTTGAAGATCATTCGGTTCAACCTT  
 GATTACCAATGACGGTGTGACCAATTGCCAAAGAAATCGAATTGGAAGACCAATTTGAAAATATGGGTGCT  
 AAGTTAGTATCAGAAAGTAGCTTCTAAAACCAATGATATCGCAGGTGACGGGACTACGACTGCAACAGTCT  
 TGACCGAAGCTATCGTCCGTGAAGGAATCAAAAACGTCACAGCAGGTGCAAAATCCAATCCGTTATCGTGC  
 TGGGATTGAAACAGCAGTTGCCGACGAGTGAAGCTTTGAAAAACAACGCCATCCCTGTTGCCAATAA  
 AGAAGCTATCGTCAAGTTGCAGCCGTATCTTCTCGTTCTGAAAAAGTTGGTGAGTACATCTCTGAAGCA  
 ATGGAAGAAAGTTGGCAAGACGGTGTATCACCATCGAAGAGTCAAGTGGTATGGAAACAGAGCTTGAA  
 GTGGTAAGAGGAATGCAGTTTGACCGTGGTTACCTTTACAGTACATGGTGACTGATAGCGAAAAATGG  
 TGGCTGACCTTGAAAAATCCGTACATTTTGATTACAGACAAGAAAAATTTCCAATATCCAAGAAATCTTGGC  
 ACTTTGGAAGCAATCTTCCAAAGCAATCGTCCACTCTTGAATTTGCGGATGATGTGGATGGCGAGGCT  
 CTTCCAACTCTTGTTTTGAACAAGATTCTGGAACTTCAACCTAGTAGCAGTCAAGGCACCTGGTTTGG  
 TGACCGTTCGCAAGCCATGCTTGAAGATATCGCCATCTTAACAGGCGGAACAGTTATCACAGAAGACCTT  
 GGTTCTGAGTTGAAAGATGCGACAATTGAAGCTCTTGGTCAAGCAGCGAGAGTGACCGTGGACAAAGAT  
 AGCAGGTTATTGTAGAAGGTGCAGGAAATCCTGAAGCGATTCTCACCGTGTGGCGTTATCAAGTCTC  
 AAAATGGAAGCTACAACCTTCTGAATTTGACCGTGAAAAATTGCAAGAACGCTTGGCCAAATTGTCAGGTGG  
 TGTAGCGTTATTAAGGTTGGAGCCGCAACTGAAACTGAGTTGAAAGAAATGAAACTCCGCAATTGAAGA  
 TGCCCTCAACGCTACTCGTGCAGCTGTTGAAGAAAGTATTGTTGACAGGTGGTGAACAGCTCTTGCCAAT  
 GTGATTCCAGCTGTTGCTACCTTGAATTGACAGGAGATGAAGCAACAGGACGTAATATTGTTCTCCGTG  
 CTTTGGAGAAGCCGTTCTCAAAATTGCTCACAATGCAGGATTTGAAGGATCTATCGTTATCGATCGTTT  
 AAAAATGCTGAGCTTGGTATAGGATTTAAGCAGCAACTGGCGAGTGGGTTAATCATGATTAATCAAGGT  
 ATCATGATCCAGTTAAAGTGAGTCTGTTGAGCCCTACAAAATGCAGCATCTGTAGCCAGCTTGATTTTGA  
 CAACAGAAAGCAAGCTGAGCCAATAAACAGAACCAAGTACCCCAAGCTCCAGCAATGGATCCAAGTATGA  
 TGGGCGGATGATGCTCGAGCACCACCACCACCACCTGA

Fig 119

## 2 CFE105 "homologue of SEQ. ID NO. 101"

ATGATTAGATTGAACCGTATTAGATATTTAAAGAAAGATGGCCTTTTTCGCGAAATATTGACCAAG  
 GTCATTACCACTACAACCTACAGCAAAGTTATTTTATAGCATCAGCTACGACAGCCGAAAGTAACAGA  
 AGACACTCTTTTGTGCAAAAGGCGCTGCCTTTAAAAAGAAATACCTTCTTCTGCTATAACACAAGOTT  
 TAGCTTGTATGTAGCTGAAAAGGACTACGAAGTCATATCCCTGTCTCATTTGTGAACGATATAAGAA



## 2 CFE 105 homologue of SEQ ID NO: 101 (Contd.)

Fig. 119 (Contd.)

AGCCATGAGTTTGATTGCCATGGAGTTCTATGGTAAATCCACAAGAGAACTCAAACCTCCTTGCTTTACT  
 GGTACTAAGGTAAGACAACAGCAACCTATTTGCGCTATAACATCTTATCTCAAGGGCATAGACCTGCTA  
 TGTGTGACGATGAACACAACCTCTTGATGGCGAGACTTTCTTTAAGTCAGCGTTGACAACCCCTGAGAG  
 TATGAACTCTTTGACATGATGAATCAGGCTGTGCAAAATGACCGTACCCACCTCATCATGGAAGTCTCC  
 AGTCAAGCCTATCTAGTCCATCGAGTCTATGGACTGACCTTTGATGTAGGAGTCTTTCTTAACATCACTCC  
 TGACCATATCGGCCCCGATTGAACACCCTAGCTTTGAAGACTATTTCTACCACAAGCGTCTCTTGATGGAA  
 AATAGCCGAGGAGTCATCATTAAACAGTGACATGGACCCTTCTCAGTCTTGAAGAAGACAGGTTGAAGATC  
 AAGACCATGATTTCTATGGTAGCCAATTTGATAACCAATCGAGAATTCAAAGCCTTTAGCTTTTCAGCT  
 ACGGTAAGCTCGTGGAGATTATGATATCCAATCATTTGCAACTTCAACCAAGAAAATGCAGTTGCTG  
 CTGACCTGCTTGTCTCCGTCTCGGAGCAAGTCTTGAGGACATCAAAAAAGGCATCGCTGCAACCCGCT  
 TCGTGTGCTATGGAAGTCTCACTCAGAAAAATGGAGCCAAGGCTTTCATCGACTATGCCCAATGGG  
 GATAGTCTGAAAAAACTCATCAATGTGGTTGAAACTCATCAACCGGAAAGATTGCTCTGGTCTGGGAT  
 CAACAGAAAAAAGGGAGAAAGTCGTGTAAGGACTTTGGCCTCTCTCAATCAACACCTGAGATTTC  
 AAGTCTTCTGACTGCTGATGACCCTAACTATGAAGACCAATGGCCATTGCAGATGAAATTAGTAGCTA  
 CATCAATCATCTCTGTTGAAAAGATTGCGGATCGCCAAGAAGCCATCAAGGCGGCAATGGCTATCAGAAA  
 TCACGAATTAGATGCAGTTATTATTGCGGGTAAGGGGCGGATTGTTACCAAAATCATCCAGGGCAAGAAA  
 GAATCTACCCAGGAGATACAGCCGTCGCAGAAAAATTATTCTGAGCACCACCACCACCACCTGA

## 2 CFE 106 "homologue of SEQ. ID NO. 102"

Fig. 120

ATGATCCAAATCGGCAAGATTTTGGCGGACGCTATCGGATTGTCAAACAGATTGGTGGAGGAGGCATGG  
 CGGATGTCTACCTAGCCAAAGACTTAATCTTAGATGGGGAAGAGTGGCAGTGAAGGTTCTGAGGACCA  
 ACTACCAAGCGACCCGATAGCTGTAGCTCGTTTCAGCGTGAAGCGAGAGCTATGGCAGATCTAGACCA  
 TCCTGATATCGTTCCGATAACAGATATTGGTGAGGAAGACGGTCAACAGTATCTTGCAATGGAGTATGTT  
 GCTGGACTAGACCTCAAACGCTATATCAAGGAACATTATCTCTTTCTAATGAAGAAGCAGTCCGTATCA  
 TGGACAAATCTCTCTTGGCTATGCGCTTGGCCATACTCGAGGAATTGTTCACAGGGACTTGAAACCTCA  
 AATATGCTTTTGACACCAGATGGGACTGCCAAGTGCAGACTTTGGGATTGCTGTAGCTTTGCGAGAG  
 ACAAGTCTGACCCAGACTAACTCGATGTGTGGGCTCAGTTCACTTGTTCACAGAGCAGGCGCGTGGTT  
 CGAAGGCGACTGTGCAGAGTGATATCTATGCCATGGGGATTATTTCTATGAGATGTTGACAGGCCATAT  
 CCGTTATGACGGGGATAGCGCGGTGACCATTTGCCCTCCAGCATTTCCAGAACCCCTGCGGTGCGTTATTO  
 CAGAAAAATTCATCTGTACCTCAGGCTTTAGAAAAATGTTATATCAAGGCAACTGCTAAAAAOKTOACCA  
 TCGCTATCGCTCGGTTTCAGAGATGTATGTAGACTGTCTAGTAGCTTGTCTCAATCGTAGAAAAAGAAA  
 GTAAGTTAATGTTGATGAAACGAGCAAGGCAAGGACAGATACCAAGACCTTGCCGAAGGTTTCTCAGAGTACCTT  
 GACATCTATCTTAAGGTTCAAGCGCAGACAGAACCAAAATCAATCAAAAAACCCAGGCGGTGAC  
 AAGGAAACTTACCAACCAAGCAGCCGAAAAAACAATAGATTTAAGATGCGTTACCTGATTTGTTGGCC  
 AGCCTTGTTATTGGTGGCAGCTTCTCTATTGATGACTATCCAGAACTCTGCAACCATTTGCCATTCCAGA  
 TGTGGCAGGTCAGACAGTTGCAAGGGCCAAAGGCAAGGCTCAAAAAAGCCAATTTGAGATTGTTGAGGA  
 GAAGACAGAGGCTAGTGAAGAGGTGGAAAGGCGGATTATCCGTACAGATCCTGGGCGTGGAACTGG  
 TCGAAAAGAAAGGAAAGAAAATTAATCTGTTGTCTCATCAGGCAAAACAATCCTTCCAAATTAAGTAATTAT  
 GTGGGCGGAAATCTTCTGATGTTATCGCGGAATTAAGAGAGAAAAAGTTCCAGATAATTTGATTAAAA  
 TTGAGGAAGAAAGTGAATGAAAGTGAGGCTGGAACGGTCTGAAGCAAAGTCTACCAGAAGGTACG  
 ACCATGACTTTGAGCAAGGCAACTCAAATGTTTGGACAGTAGCTAAAAAGCTACGACGATTCAATTAG  
 GGAATATATTGGACGGAACCTCTACAGAAAGTAATCTCAGAACTCAAGCAGAAAGAGGTCTCTGAGAATT  
 TGATTAGATAGAGGAAGAAGAGTCCAGCGAAAGCGAAACGGAACGATTATGAAACAAAGTCCAGGT  
 GCGGAAACGACTTATGATGTGAGTAAACCTACTCAAATTTGCTTGCAGTAGCTAAAAAAGTTACAAGTG  
 TTCCATCCGAGTTACATTGTTCCAGCTTGGAGTTTACTAAGAACAATTTGATTCAAATTTGTTGGGATT  
 AAGGAACTAATATAGAAGTTGTAAGAGTGACGACAGCGCTGCAGGTAGTGTAGAAGGCATGGTTGTT  
 GAAACAAAGTCTAGAGCAGGTGAAAAGGTAGACCTAAATAAGACTAGAGTCAAGATTTCATCTACAAA  
 CCTAAACAAGTTCACTACTCTGCGGCGCACTGAGCACCACCACCACCACCTGA

## 2 CFE 107 "homologue of SEQ. ID NO. 103"

Fig. 121

ATGAAACATTTGATACTATGTCATCGGTGGGGACCTGCTGGTATGATGGCTACGATTTCCAGTAGCTT  
 TTATGGACAGAAACCCTCTCATCGAAAAAATCGGAAACTTGGAAAAAATAGCTGGGACTGOTGG  
 GGGACGTTGCAATGTGACCAACAATGTAGCTTAGACAACCTGCTAGCTGGAATTCCTGGAACGGACG  
 CTTCTTTACAGTGTCTTCTCCAGTTTCGATAATCATGACATCATCAACTTTTTACAGAAAAATGGTGTAA  
 ACTTAAGGTGGAAGACCAGGACGCGCTTTTCCAGCAGTGACAAGTCTCGGACTATTATCGAAGCTTTG  
 GAAAAAGAAATCACTGAACAGGTGGTCAAGTTGCTACTCAAATAGAAATCGTTTCTGTTAAAAAAGTA

2CFE 107 (Contd)

Fig 121 (Contd)

GATGACAGTTTGTCTTAAGTCAACGGATCAAACTTCACTTGTAAAGAACTCATTGTGACAAACAGGTG  
 GTAGTCTTATCCTTCGACTGGTTCCGACTGGCTTTGGTCACGAGATTGCTCGCCATTTAAGCATACCATC  
 ACCGATCTTGAAGGCTGCTGAAAGTCTTTATTAACAGATTTTCCACATAAAGCCTTACAAGGGATTTCCT  
 GGACGATGTGACCCTAAGTTATGGTAAGCATGTGTCATCACTCATGATTACTCTTTACCCACTTTGGTTGT  
 CAGGTCTGTGCTGCCCTACGCATGTCTAGCTTTGTCAAAGGTGGGGAGGTCTCTCACTCGATGTTTGCCT  
 CACTTTCTGAGAAGGACTTGGTTACATTTCTAGAAGAAAAATCGGGAAAAATCCTTGAAAAACCGCTTAA  
 AAACCTTGTGTTACCAGAACGCTTGGCCGAATTTTTGTACAAGGATATCTGAAAAAGTCAAAACAGCTGAC  
 TBAAGGAAAGGAAACGAGAACAACTTGTCCAGTCCATTAAAGAACTTAAATTCCTGTAACCTGAAAAATGTC  
 CCTTGCAAAAGTCTTTGTTACCAAGGGTGGAGTCAGTCTCAAGGAAATCAATCCTAAACCTTGAAAGT  
 AAGCTGTACCTGGCCCTCCACTTTGCAGGCAAGTTATGGATATCAATGCCACACGGGTGGCTTTAACA  
 TCACTTGTGCCCTCTGTACCGGCTGGGTGGCGGGAAGTCTGCATTATGATCTCGAGCACCACCAACCA  
 CCACTGA

Fig 122

## 2 CFE108 "homologue of SEQ. ID NO. 104"

ATGCTGAAATGGGAAGACTTGCCTGTGGAAATGAAATCAAGCGAGGTTGAGTCTTACTACCAGCTTGTCT  
 CTAAAAGGAAGGGTTTCGCTGATTTTCAAGCGTTTGGCTTGGACTGGGTTTGGCCTTGGCTTACTGGTTCTA  
 ACTTCTCCCATCTTTCTCATCTTGAGCATTGGATCAAGTTGGATAGCAAGGGGCCAGTGATTACAAGCA  
 AGAGCGTGTGACCCAGTACAACCGTCCGTTCAAGATTGGAAGTTCGTACCATGGGTGACGGATGCGGAT  
 AAAAAAGGAAGTCTGGTGACTTCTGCTAACGATAGCCGATTACCAAGGTTGGAAATTCATCCGACGTG  
 TCGGTTGGACGAACTGCCTCAATTGGTCAATGTCCTTAAAGGTGAGATGTCCTTTGTGCGGTACACGACCT  
 GAAGTGCCACGTTATACAGAGCAGTATAGCCGTGAAATGATGGCAACCTTGGCTCTTGCAAGCAGGAATTA  
 CCTCTCCAGCCAGCATCAACTACAAGGATGAGGACACCATCATCAGTCAAATGACGGAGAAAGGTCTGT  
 CAATTGATCAGGCCTATGTGGAGCATGTTCTTCTGAAAAAGATGCGCTATAACCTCGCTATCTCCGAGA  
 GTTAGTTCTTTGGGGACATCAAAATCATGTTTCAAAACCGTGTGTTGAGGTACTAAAACCTCGAGCACCACC  
 ACCAACCACCTGA

Fig 123

## 2 CFE109 "homologue of SEQ. ID NO. 105"

ATGACTAGTCCACTATTAGAATCTAGACGCCAACCTCGTAAATGCGCTTTTCAAGCTCTCATGAGCCTTGA  
 GTTCGGTACGGATGTGCAAACTGCTTGTGCTTTCGCTTACTCATGATCGTGAAGATACGGATGTACAA  
 CTTCACGCTTTTGTATAGACCTCGTTCTGTGTTCAAGCTAAAAAGGAAGAACTAGATAAGCAAAATCA  
 CTCAGCATTTAAAGCAGGTTGGACCATTAACGCTTAAACGCTCGTGGAGAGAAACCTCTCGCTTGGG  
 AGTCTTTGAAATCACTTCATTGACACTCCTCAGCTGCTGTTGCTGTTAATGAAGCTATCGAGCTTGCAAAAG  
 ACTTCTCCGATCAAAATCTGCCCGTTTTATCAATGGACTGCTCAGCCAGTTTGTAAACAGAAGAACAAT  
 CGAGCAACCACCACCACCACCTGA

Fig 124

## 2 CFE111 "homologue of SEQ. ID NO. 107"

ATGACAAAACGTGTAACGATTATGATGTAAGAACTATGTTGGTCAGGAAGTGACGATTGGCGCTTGGG  
 TTGCCAACAAATCAGGAAAAGGGAATCGCTTTCTTACAATTGCGTGATGGAACAGCCTTCTTCAAGG  
 TGTACTTTTAAACCAAACTTTGTGCAAAAAATTTGGTGAAGAAGTGGGACTTGAGAAGTTGATGTTATC  
 AAACGCTTGAGCCAAGAAACGCTCTGTTATGTGACAGGTATTGTCAAAGAGGACGAACGTTCTAAATTTG  
 GCTATGAGTTGGACATCACAGACATCGAAGTGATCGGTGAATCTCAAGACTACCCAATCACACCAAAAG  
 AACACGGAACAGACTTTTGTATGGATAACCGTCACTTGTGGCTACGCTCTCGTAAGCAAGTAGCTGTGT  
 GCAAAATCGTAACGCTATTATCTATGTAACCTATGAGTTCTTTGACAAGAAATGGTTTATGAAGTTTGACA  
 GGGCAATCTTTTCAGGAAATGCGGCAGAAAGATTCTACAGAACTCTTTGAAACTGACTACTTCGGAACGCC  
 AGCCTACTTGAGCCAATCAGGTCACTTTACCTAGAAGCAGGGGCTATGGCTCTTGGTCTGTTGACT  
 TTGTTCCAGTTTTCGCTGTGAAAAATCAAAAAACGCCGTCACTTGACTGAGTTCTGGATGATGGATGC  
 TGAGTACTCATACTTGACACATGATGATCGCTTGACTTGCAAGAAAGCTTATGTGAAAGCTCTTCTACAA  
 GGTGTTCTTGACCGCGCGCTCAAGCCTTGGAAACCTTGGAACTGATACAGAACTCTTGAAACGCTACA  
 TTGACAGGCCATTCAAACGTATCACTTACGATCAAGCCATTGACCTCTTGCAAGAGCATGAAATGATGA  
 AGATGCTGACTACGAGCATCTTGAGCATGGTGATGACTTTGGGTCAACACAGGAACTTGGATTTCAAAC  
 CACTTGTGTGCAACATTTGTGATGAATATCCAGCAGCCATCAAGGCCTTCTACATGAACCACTTCC  
 TGGAAATCCAGAGCGCGTCTTTGTGACAGCTTGTGCTCCAGAGGCTATGGAGAAATTAAGGTGGG  
 TCTATGCTGAGGAAGATTACGATGCCCTTGTGCTAAGATGGATGAACTTGGCATGGATCGTACAGAAT  
 ATGAATTTACCTTGACCTTCGFAAATACGTTACAGTCCACACGGAGGATTTGGTATCGGTATCGAAG  
 TATGGTAACCTTCGACGAGGAACAAAAATATCCGTGAAGCTATTTCAATCCACGTATGTTGACCGT  
 ATCAAACTCTGAGCACCACCACCACCACCTGA



## 2 CFE112 "homologue of SEQ. ID NO. 108"

ATGTCCTGAAAAATTAGTAGAAATCAAAGATTTAGAAATTTCTTCCGCTGAAGGAAGTAAGAAGTTTGTGCG  
CGGTTAAAAATGCTAACTTCTTTATCAACAAGGGAGAAACTTTCTCGCTTGTAGGTGAGTCCGGTAGTGG  
CAAAAGAACTATTGGTCGTGCTATCATCGGTCTAAATGATACAAAGTAATGGAGATATCATTTTGTATGGT  
CAAAAGATTAAATGGTAAGAAATCGCGTGAACAAGCTGCGGAATTGATTGCTCGAATCCAGATGATTTTCC  
AAGACCTGCGCGCAAGTTTGAATGAACGTGCGACTGTTGATTATATTATTTCTGAAGGTCTTTACAATCAC  
CGTTATTTAAAGGATGAAGAAGAACGTAAAGAGAAAGTTCAAAGTATTATCCGTGAAGTAGGTCTTCTTG  
CTGAGCACTTGACTCGTTACCTCATGAATTCTCAGGCGGTCAAAGTCAAAGTATCGGTATTGCCCGTGCC  
TTGGTCATGCAACCAGACTTTGTTATTGCAGATGAGCCAATTCAGCCTTGGACGTTTCTGTACGTGCCCA  
AGTCTTCAACTTGTCAAAAAATTCAAAAAGAGCTCGGCTTGACCTATCTCTTCATCGCCCATGACTTGT  
CGGTTGTCGCTTTATTTTCAGATCGTATCGCAGTTATTACAAAGGTGTTATTGTAGAGGTTCAGAAACA  
GAAGAATTGTTTAAACAATCCAATTCACCCATATACTCAAGCCTTGCTTTACGCGGTACCAATCCAGATCC  
AATCTTGAAAGGTAAAGAAGGTCTTGAAGGTTTACGACCCAAGTCAACACGACTATGAGACTGATAAGCC  
ATGATATGTAAGAAATCCGTCCAGGTCACTATGTTTGGGCGAACCAGCTGAATTAGCACGTTATCAAAAA  
GGACTAAACCTCGAGCACCACCACCACCACCCTGA

## 2 CFE113 "homologue of SEQ. ID NO. 109"

ATGAAGATAAGTTGGAATGGATTCTTAAAAAATCATACCAAGAGCGCCTCGAGCTGCTAAAAAGCTCAG  
GCGCTCTTAGTCTGTAGAGACAAGCTAGTCTGGAGAAGGATGAACAGATGAGTGTGACTGTGGCAGAC  
CAGCTGAGTGAGAATGTGGTGGAACTTTTCTCTGCTTATTCGCTGGTTCGCGAAGTACTTGTCAACGG  
TCAGGAATACACCGTTCCCTATGTGACAGAAGAACCCTGTGTTGCGGCGGCCAGCTATGCCAGCAAA  
ATGATCAAGCGTGCAGGTGGTTTACTGCAACAAGTCCATCAGCGCCAGATGATTGGGCAGGTAGCCCTTT  
ATCAAGTTGCTTAATCTAACTAGCGCAAGAGAAGATTGCCAGCAAGAAAGCGGAGCTCTTGAGCTTG  
CCAATCAAGCCTATCTCTATCTGTTAAACGTGGGGGTGGGGCGCGTGATCTGCATGTGAGCAGATAAA  
AGCGGAACCAAGACTTTCTCGTTGTTTATATTCTATGTCGATACCCAGGAAGCCATGGGTGCCAATATGCTC  
AAGACCAATGCTGGAAGCCTTGAACCCAGTCTTAGAAGAACTCAGTCAGGGACAGAGTCTCATGGGAATC  
CTGTCCAACCTACGCGACTGATTCTCTGGTGACTGCAAGCTGTGCGCATCGCCTTTCGCTACTTGAGCCGCCA  
AAAGGATCAAGGACGAGAGATTGCGGAGAAAATTCGTTGGCTAGTCAGTTTGGCGAGGCTGATCCTTA  
CCGAGCTGCTACTATAATAAAGGAATTTTAAATGGTATTGATGCGATTTTGATTGCCACTGGTAATGACT  
GGGGTGGCATCGAAGCTGGGGGCCATGCCCTTGGCAGTCGAGATGGACGCTATCAAGGTCTTACGTGCTG  
GAGGCTGACCTTGAAGAGAAGAATTGGTGGTGAGATGACCTGCCCATGCGCTGTAGCGACTAAGGG  
TGGCTCTATCGGCTCAACCCACGTGTAGCTCTCAGTCATGATCTACTAGGAAATCCTTCTGCCAGAGAAT  
TAGCCCAAGATTATCGTGTCCATCGGTCTTGGCTCAAAATTTTGCAGCCCTCAAAGCCTTGGTAAGTACGGGC  
ATCCAGCAAGGCCACATGAAACTACAGGCCAAATCCCTAGCTCTCTAGCTGGGGCTAGTGAATCTGAAG  
TTGCTCCCTAGTAGAGCGCCTCATCTCAGATAAAACCTTTAACTAGAGACAGCCAGCGCTATCTCGA  
AAATTTAAGATCAGCGGCCGCACTCGAGCACCACCACCACCACCCTGA

## 2 CFE114 "homologue of SEQ. ID NO. 110"

ATGCCAATTACATCATTAGAAATAAAGGACAAGACTTTTGAAATCGATTGAGAGGTTTGTATCCAGAAAG  
AAGTCGATGAATTTTATAGATATTGTGGTTCTGTGATTACGAAGATCTTGTGCGTGCGAATCATGATAAAAA  
TTTGGCTATTAAAGAGTTTAAAGAGCGTTTGTCTTACTTTGATGAAATAAAGATTCAATTGAGCCAGTCTG  
TATTGATTGCTGAGGATACAGCTGAGAGAGTGAACAGGCGCGCATGAACGTTCAAACAATATCATTC  
ATCAAGGAGAGCAAGATGCGCAACGCTTGTGGAAGAAGCTAAATATAAGGCAAAACGAGATTCTTCTGTC  
AAGCAAGTGATAATGCTAAGAAAGTCCGCTGTTGAACAGAAAGATTGAAGAACAAGAGCCGTGTCTTCC  
ACCAACCTCTCAAATCTACAATTGAGAGTCAAGTTGGCTATTGTTGAATCTTCAGATTGGGAAGATATTCTC  
CGTCCAACAGCTACTTATCTTCAAACAGTGATGAAGCCTTTAAAGAAGTGGTTAGCGAAGTACTTGGAG  
AAGCAATCCAGCTCCAATTGAAGAAGAACAATTGATATGACACGTCAGTTCTCTCAAGCAGAAATGGA  
AGATTACAAGCTCGTATTGAGGTAGCCGATAAAGAATTGCTGAAATTGAAGCTCAGATTAAACAGGA  
AGTGAAGACTCAACTCTGTAGTGTGAGTCCCTCAAGTTGAAGAAGAGCCTCTGCTCATCCAGTTGGCCCAA  
TGATTAAGAACCAGAAAGCTCGAGCACCACCACCACCACCCTGA

## 2 CFE115 "homologue of SEQ. ID NO. 111"

ATGCTAATGGACAACATAATTATTTAATGGTTGCAATTGCAGTCATTTAGTTCTGGCTTATGTAGTGGC  
AATCTTTCTACCTAAGCGAAACGAGGGGAGATTAGAGGCGCTAGAAGAAAGAAAAAGAACTATACA  
ATCTTCCAGTAAATGATGAAGTGAAGCTGTAAAAAATATGCACCTTGATTGGACAAAGTCAAGTGGCTTT

2CFE 115 (Contd)

Fig 128 (Contd)

CCGTGAATGGAATCAAAAATGGGTGCGATTATCTCTCAACTCTTTGCCGATATTGAAAAATAATCTCTTGG  
 AAGCAGAAAGGCTATAACCAATTCATTTCTGTTTCTCAAGGCCAGTCATCAAATTGACCAAATTGAGAGTCA  
 AATTAGTTTGATTGAAGAAGATATTGCGGCAATTCGCAATGCTTTGGCAGACTTAGAGAAGCAAGAATCT  
 AAAAAATAGTGGTCTGTTCTTCATGCTTTGGATTATTTGAGGAACTTCAGCATAGAGTTGCTGAAAAATTC  
 AGAACAGTATGGTCAAGCCTTGGATGAAAATTGAAAAACAATTAGAAAATATCCAATCTGAATTTTCACAA  
 TTTGTAACTTGAATTCATCGGGTGACCTGTGGAAGCCGCGAGTGATTTGGATAATACAGAAAAATCACA  
 TTTTGGCCTTAAAGTCATATTGTGGATCGTGTTCAGCCTTGGTTACGACGCTTTCTACAGAAATTGCCAGAT  
 CAATTACAGGATTTGGAAGCCGGTTATCGTAAACTAATTGATGCTAATTATCATTTTGTGAAACCGGATAT  
 TGAAGGCGTTTCCACTTGCTTTATGAAGCATTCAAGAAAAACCAAGAGAATATTGTCAGTTGGAATTG  
 GATAATGCGCAATATGAGAATGGACAGGCACAAGAGGAAATCAATGCCCTGTATGATATTTTACTCGAG  
 AAATTGCTGCTCAGAAAAGTAGTGGAAAAATCTACTTGGCAACTCTTCCAACCTACCTTCAACATATGAAAGA  
 GAATAATACTTTATTGGGAGAAGATATTGCACGTTTGAACAAGACCTATTTACTTCTGAGACAGCTGCA  
 AGCCATGTTCTGCTGATTTCAGACAGAATTAGAGAGTTTGAAGGCAGCTATTGTTGAGGTAACCTTCAAATC  
 AAGAAAGAACCAACCAAGCTTATTCAGTTCTTGAAGAAAATCTTGAAGGATTTACAAACTCAACTAAAAAG  
 ATATTGAAGATGAGCAAAATTCAGTTAGTGAGCGCTGACACAAATTGAGAAAGATGATATTAATGCAC  
 GTCAAAAAGCCAATGTTTATGTCAATCGTCTCCATACTATCAAGCGATACATGGAAAAACGCAATCTGCC  
 AGGATTCACAAAACCTTCTTGAAGTTATCTTTACGGCAAGCAATAATACCGAGGATTTAATGGTTGAGT  
 TAGAACAACAAAATGAATTAACATTGAATCTGTACCCGAGTTCTTGAATTTGCAACGAATGATATGGAAGC  
 TTTAGAACGGAAACTTATAATATTGTACAATATGCAACTTTGACAGAGCAACTCTTGAATATTCTTAAC  
 CGCTATCGCTGATTTGATGAACGCATTCAAGAAGCATTTAACGAAGCTTTAGATATTTTGAAGAAAGAT  
 TTGATTATCACGCTTCATTTGACAAGATTCTCAAGCATTGAAGTGGCAGAGCCTGGTGTAAACCAATCG  
 CTTTGTACCTCATATGAGAAAACACGTGAAACGATTCTGTTTGGCGCCGCACTCGAGCACCAACCAACAC  
 CACCACTGA ||

Fig 129

2 CFE116 "homologue of SEQ. ID NO. 112"

ATGCTTATATCTTATAAATGGTTAAAGAAATGGTGGACATTGATGTGCCATCACAAGAGTTGGCTGAAA  
 AAATGTCAACTACAGGAATCGAGGTAGAGGGTGTGCAATCACCAGCTGCTGGTCTCTCAAAAATTGTCGT  
 CGGTGAGGTCTTGTCTTGGCAAGATGTGCCAGAGACTCACCTCCATGTTTGTGAGGTTAACGTTGGCGAA  
 GAAGAGCGTCAAGTCTTTGTGGTGCCCCAAATGTGCGTGTGGGATCAAGGTCATGTTGGCTCTTCCAG  
 GAGCTCTATGCTGATAACTACAAAATCAAAAAGGAAAAATCCGTGGTTTGGAGTCACTTGGAAATGA  
 TCTGTTCACTTGGTGAATTGGGAATTTCTGACTCAGTTGTGCTAAGGAATTGCGCATGGCATCCAAATC  
 TTGCTGAAGATGCCGTGCCAGGTGAGGAAGTCTTTTCTTACCTAGACTTGGATGATGAAATCATCQAAC  
 TTCCATCACACCAAACCGTGCAGATGCCCTTTCTATGTGTGGAGTGGCTCACGAAGTGGCAGCCATCTA  
 TGACAAAGCAGTCAACTTTAAAGAAATTTACTCTAACAGAACTAATGAAGCTGCGGCAGATGCCCTTTCT  
 GTGAGCATTTGACAOACAAGGCGCTTACTATGCAGCTCGTATCTTGGACAAATGTQACCATCGCACCAA  
 GTCCACATGCTTGCAAAACCTTCTCATGAACGAAGGAATCCGTCCCATCAATAACGTAGTGGACGTGAC  
 CAACTAGATCTGCTATTTTGGTCAACCAATGCATGCCCTTGGACTTGGATAACTTTGAAGGGACTGACA  
 TCGGTGTGCGTGAAGCGCGTGTGGTGA AAAAATTTGGTGACCTTGGACGGTGAAGAACGTGACTTGGACGT  
 GAATGACCTAGTCATCACTGTGCGAGACAAGCCAGTAGCCCTTGCAGGTGTGATGGGTGGTCAAGCAACA  
 GAAATCTCTGAAAAATCTATGCTGTGTCTTGAAGCTGCTGTTTCAATGGCAAATCTATCCGTAAGAC  
 AAGTGGTCCGCTGAACCTTCGTTCTGAGTCACTTCTCGCTTTGAAAAAGGAATTAATGTGGCAACAGTT  
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2CFE 116 (contd)

Fig 129  
(contd)

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Fig 130

2 CFE117 "homologue of SEQ. ID NO. 113"  
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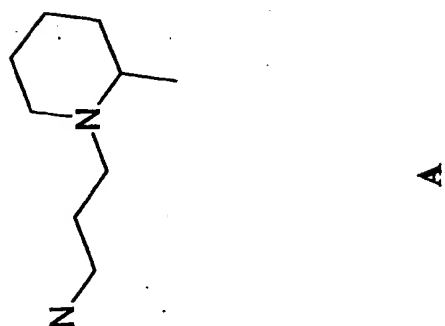
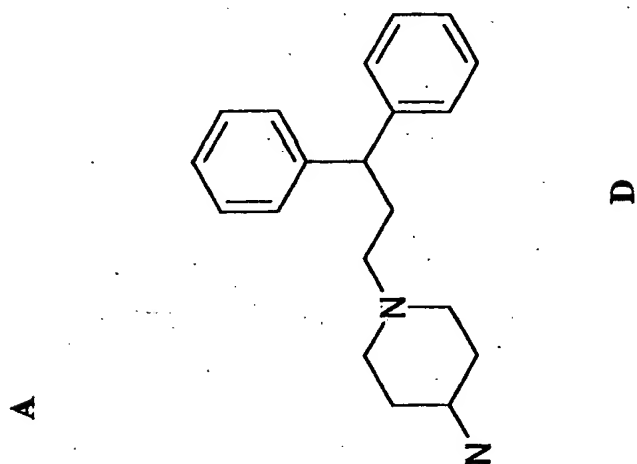
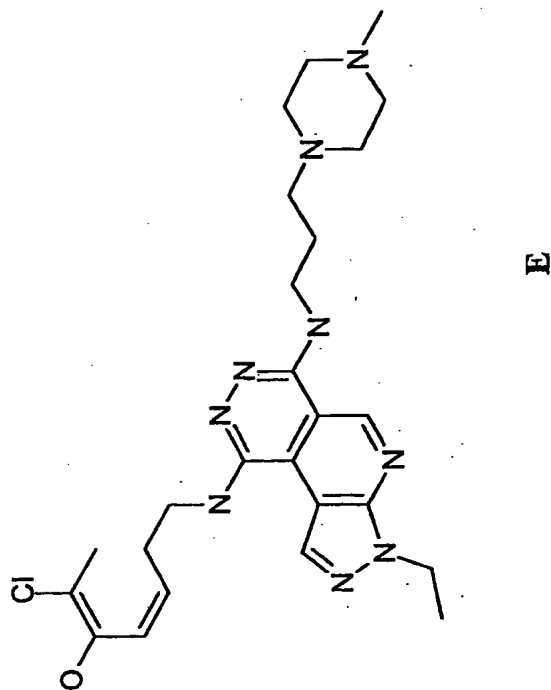
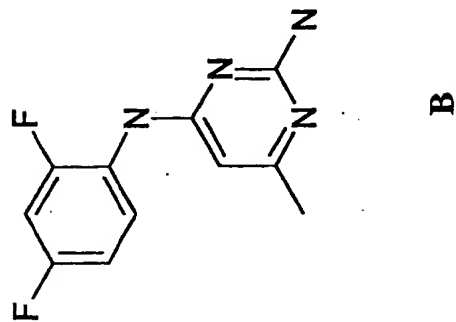
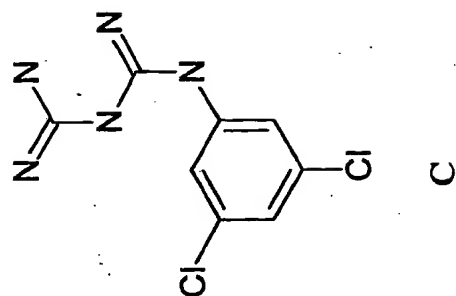


FIGURE 131

## SEQUENCE LISTING

- <110> Dougherty, Thomas J.  
Pucci, Michael J.  
5 Dougherty, Brian A.  
Davison, Daniel B.  
Bruccoleri, Robert E.  
Thanassi, Jane A.
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&lt;213&gt; Streptococcus pneumoniae

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&lt;211&gt; 720

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&lt;213&gt; Streptococcus pneumoniae

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&lt;213&gt; Streptococcus pneumoniae

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 20 gtataa 846

&lt;210&gt; 26

&lt;211&gt; 1290

&lt;212&gt; DNA

25 &lt;213&gt; Streptococcus pneumoniae

&lt;400&gt; 26

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 35 gcccgcttga atgccttctt tgctaacttc cgctctgttg acgaagaatt tttcgaggaa 480  
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 atgaaaggct tcttggaagg tttaatctaa 1290

&lt;210&gt; 27

&lt;211&gt; 498

&lt;212&gt; DNA

&lt;213&gt; Streptococcus pneumoniae

55

&lt;400&gt; 27

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caagaaatTT tggaattgc agccaaaaa ttaggaaaag aagacaagga gatggcagtc 120  
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 5 gaattgttca tctctatcga taaggctcat gagcaggccg aagaatatgg toacagcttt 360  
 gagcgtgaga tgggcttctt ggcagtacac ggctttttac atattaacgg ctatgatcac 420  
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10 <210> 28  
 <211> 768  
 <212> DNA  
 <213> Streptococcus pneumoniae

15 <400> 28  
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 ccaggcttgg tagctcatca ggaagtcac tttggcaatc agggagaagg gttgaccctc 660  
 cgtcatgact cctatgatcg catctccttc atgacaggag tcaatttggg aattaaagaa 720  
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30 <210> 29  
 <211> 276  
 <212> DNA  
 <213> Streptococcus pneumoniae

35 <400> 29  
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 gaaaaagttc agttgatcgg ttttagtaac tttgaagttc gtgagcgcgc agaacgtaaa 180  
 ggtcgcaacc cacaactgg taaagaaatg acaattgcag cttctaaagt accagcattc 240  
 40 aaagctggta aagctcttaa agacgctggt aaataa 276

<210> 30  
 <211> 921  
 <212> DNA

45 <213> Streptococcus pneumoniae

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 atgcaagaag caggcataag caactttatc gagattggac cggggaaagt cttgtcaggt 840  
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 gtagcacttt tagaaaaata g 921

<210> 31

<211> 732

10 <212> DNA

<213> Streptococcus pneumoniae

<400> 31

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 tcagaagaat tgctcgctga gttttcaaac tatggatca aggtggttcc catttcagga 180  
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 20 acagaagcag attttgaaaa agtgctcaag gtcaatctga ctggtgcctt taatatgaca 360  
 caatcagctc tgaaccgat gatgaaagcc agagaagggt ctatcattaa tatgtctagt 420  
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 gctacactag ctcagattcc gatgaaagaa tttgggcagg cagagcaggt tgcagatttg 660  
 25 acagtatttt tagcaggcca agattatcta actggtcaag tgggtgccat tgatggtggc 720  
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<210> 32

<211> 831

30 <212> DNA

<213> Streptococcus pneumoniae

<400> 32

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 agtaaatgg tttacttctt tgcggaaatc attcgctttt tatcgtttga tattagtatc 180  
 ggagtgggga ttattctctt tacggtcttg attcgtacag tctcttggc agtctttcag 240  
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 45 ggtggagtgc cctatactg gacagtgtct aatgcttata aagtcttgca aacctatttc 720  
 ttgaataatc cattcaagat tatcgagag cgcgaggccg tagtacaggc acaaaaagat 780  
 ttgaaaaata gaaaaagaaa agccaagaaa aaggctcaga aaacgaaata a 831

<210> 33

50 <211> 1230

<212> DNA

<213> Streptococcus pneumoniae

<400> 33

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 aatcaaccaa tgaaccttct gttgaagtag 1230

20 <210> 34  
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 <212> DNA  
 <213> Streptococcus pneumoniae

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 45 cgccgcaaac cattgaaaca agaaattgaa acctatgtca ccttggccgg agtggctatc 1200  
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<210> 35  
 <211> 594  
 50 <212> DNA  
 <213> Streptococcus pneumoniae

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 aatcaggagg ctcagattta tgtgcatcag gttgtcgtg aggaagccca tttgctttat 180  
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 aaggtcgcag tgcaagcaag tgctgaaaac caagaattgg aagaagctat ggaagccatg 480  
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<210> 36

<211> 774

10 <212> DNA

<213> Streptococcus pneumoniae

<400> 36

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 gaattattat cgggtcagga aattaaaaac ttggaagaca tgaaaactgc agcgagaaa 480  
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 25 aaagtgata aatttttggc agcagtagaa agctctaagg ctttcgttta tctgtctatt 720  
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<210> 37

<211> 1239

30 <212> DNA

<213> Streptococcus pneumoniae

<400> 37

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<210> 38

<211> 483

&lt;212&gt; DNA

&lt;213&gt; Streptococcus pneumoniae

&lt;400&gt; 38

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 accattgaaa cgctgttggt tagctatgat gtaaaaatct tgaaggttga aaaaacagcc 480  
 taa 483

15 &lt;210&gt; 39

&lt;211&gt; 570

&lt;212&gt; DNA

&lt;213&gt; Streptococcus pneumoniae

20 &lt;400&gt; 39

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 ttacagtctg ttgacaaaagt tgacgattct gtaaaactact atttacaaga gaaaaatttt 540  
 30 gagaaaacaa tgcagaggta taacggataa 570

&lt;210&gt; 40

&lt;211&gt; 852

&lt;212&gt; DNA

35 &lt;213&gt; Streptococcus pneumoniae

&lt;400&gt; 40

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 40 atggttgaga aagtttttga agaggtgaaa ccgacttttag tctaccattg tgcagcctac 180  
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&lt;210&gt; 41

55 &lt;211&gt; 1224

&lt;212&gt; DNA

&lt;213&gt; Streptococcus pneumoniae

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 <212> DNA  
 <213> Streptococcus pneumoniae

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 agaaaaacct gtggtcgtct gtttgaggct ttagtacagc actttgggca agaaatcatt 180  
 35 cttgaaaaac gagaaactcaa tcgccctctc atagctagtc tcatcttttc aaatcctgaa 240  
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&lt;210&gt; 44

15 &lt;211&gt; 696

&lt;212&gt; DNA

&lt;213&gt; Streptococcus pneumoniae

&lt;400&gt; 44

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 25 gatttacaat gtgagtatat ttgtattcat gctgaagttc tgaatggtct tgcttttcgt 300  
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 gaagaaatga ccggaaaaac aatgccaatc aataaa 696

&lt;210&gt; 45

&lt;211&gt; 1125

35 &lt;212&gt; DNA

&lt;213&gt; Streptococcus pneumoniae

&lt;400&gt; 45

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 tacggatctg aaaaggccgt aaaagaagct ggacgcttgc gtgaagaagg aaaagaatat 1080  
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 <212> DNA  
 5 <213> *Streptococcus pneumoniae*  
  
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213> *Streptococcus pneumoniae*

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&lt;210&gt; 57

&lt;211&gt; 723

&lt;212&gt; DNA

40 <213> *Streptococcus pneumoniae*

&lt;400&gt; 57

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&lt;210&gt; 58

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 <213> Streptococcus pneumoniae

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 <213> Streptococcus pneumoniae

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 <213> Streptococcus pneumoniae

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gctgtctata gtacacttga tgtctaa 1947

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<213> Streptococcus pneumoniae

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<210> 63  
<211> 867  
<212> DNA  
35 <213> Streptococcus pneumoniae

<400> 63  
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55 <211> 420  
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<213> Streptococcus pneumoniae

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 <210> 67  
 <211> 630  
 <212> DNA  
 <213> Streptococcus pneumoniae  
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15 <210> 68  
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 <212> DNA  
 <213> Streptococcus pneumoniae

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35 <210> 69  
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 <213> Streptococcus pneumoniae

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 ttttcttggg ctgggctagg tgtttgggag caataataca aagctcaagc cttttataat 420  
 cgatatggtt ttgaaaaatt tagccaacat cattttatgg ttggtcaaaa agtagatacg 480  
 50 gattggttac tgagaaagaa attaaggtaa 510

<210> 70  
 <211> 1590  
 <212> DNA  
 <213> Streptococcus pneumoniae

55 <400> 70  
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 ttaccatgg gttacactat ctatgcttgg ttcttggttg tttcaacagc ggggattcca 180  
 gttgcggtgg ccaagcaagt tgccaagtat aataccatgc gagaagaaga gcatagcttt 240  
 5 gcccgtatgc ggagcttctt aggcctttatg acaggactag gcctggtttt tgctttagtc 300  
 ttgtatgtct ttgctccttg gctagcagac ttgtctggcg tgggcaaaga cttgatccca 360  
 atcatgcaaa gcttggcttg gggagtcttg attttcccg ctatgagtgt tatccgagga 420  
 tttttccaag ggaatgaataa cctcaaacc tatgccatga gccaaattgc tgagcaggtc 480  
 attcgtgtta tctggatgct cctagcaacc tttatcatta tgaagctcgg ttcaggagat 540  
 10 tatctagcag ccgttaccca atcaaccttt gctgcctttg tcggtatggt agccagtttt 600  
 gcagtcttga tttatttcct tgccaagaa agttcactca aaagagtctt tgaacagga 660  
 gataagatta acagtaagcg tctcttggtt gataccatta aggaagccat tccttttacc 720  
 ctgacagggt ctgccatcca gatcttcag attttgatc agctgacctt tatcaatagt 780  
 atgagctggt ttaccaacta cagcaatgag gacttggtt tcatgtttt ttattttctca 840  
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 ggacgtttgt ggagcttctt ttatgtagct cttgtcgggt ccatgggggg tggactttat 1500  
 25 atggttatga gtctgcgtac ctatttatta gataaggtaa taggaaaagc ccaagcagat 1560  
 cgctgcgag caaaatttaa gctttcgtaa 1590

<210> 71  
 <211> 468  
 30 <212> DNA  
 <213> Streptococcus pneumoniae

<400> 71  
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 ccccaacaac aaggatttct tcctatcgaa aatcgtaaac gggggctaga aaaggctttg 180  
 ggacatctgg aaaatgttga agtcgtggct tctcatgatg aattggtggt cgatgttgca 240  
 aaaagattgg gtgctacttg tctagtgcgt gggttgagga atgcgtcgga tttgcaatat 300  
 40 gaagccagtt ttgattacta caatcatcag ctgtcttctg atatagagac tatttattta 360  
 catagtgcac ctgaacatct ctatatcagt tcatcaggcg ttagagagct tttgaagttt 420  
 ggtcaggata ttgcctgcta tgttcccag agtatttga ggaaataa 468

<210> 72  
 <211> 432  
 45 <212> DNA  
 <213> Streptococcus pneumoniae

<400> 72  
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 gagcaggccg atcaggttga tttatacaat ggcttggaa cttattacag cgttcttggt 180  
 cgtaataaac agcaagaagc acttgctgtt ctgattggaa aagatgatca taagatttac 240  
 gtttatcagc taaatcaggg tgtttcacia gaaaaagcag aaacggtttc taaggaaaag 300  
 ggagctggcg aaattgacaa gattatcttt ggtcgttatc aagataagcc aatctgggaa 360  
 55 gtcaagtcag gatctgattt ttatctagta gattttgaaa caggagcatt ggtcaacaag 420  
 gagggcctat ga 432



<210> 73  
 <211> 732  
 <212> DNA  
 <213> Streptococcus pneumoniae

5

<400> 73  
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 tctcaccgtc gcaagggcat gtttgaaact ccagaagaga agatagcaga aaactttctt 180  
 10 caggttcggg aaatagctaa ggaagtcgag agtgacttgg tcattgctta tggggctgaa 240  
 atttactaca cgccagatgt tttggataag ctggaaaaca atcggtattcc gacctcaat 300  
 aatagtcgtt atgccttgat agagttagt atgaacactc cttatcgca tattcatagt 360  
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 gatgttcttg aaaataatga aaaacgcgtt cgagagctga tcgatatggg ctgttacacg 480  
 15 caaataaata gttcacatgt cctcaaatcc aaactttttg gagaacctta taaattcatg 540  
 aaaaaagag cgcagtattt cttggagcgt gatttgggtc atatcattgc aagtgatatg 600  
 cataatgtgg acggcagacc ccccatatg gcagaagcat atgacctgtt tccccaaaaa 660  
 tacggagaag cgaaggctca ggaacttttt atagacaatc ctgaaaaat tgtaatggat 720  
 caactaattt ag 732

20

<210> 74  
 <211> 927  
 <212> DNA  
 <213> Streptococcus pneumoniae

25

<400> 74  
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 aaatcaactg tagtcatgtt gggaatcttg gtagccatca ttttgataag tttcatctac 180  
 30 ccaatgtttt ctaagtgtga tttcaatgat gtcagcaagg taaacgactt tagtgttctg 240  
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 aacttgggtt tcggtgtttt tgtcgggtgt atttgggtta tttcaaaatc agttgacgt 420  
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 35 ttgacttact caatcgagc tggattctgg aatctgattt ttgccatgag cgtacaaca 540  
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 tacgaagcct tcttgtcttt cttcgggtct ggattaccga ttacagtgc aagtttgggt 780  
 40 cgtttgattt cggattattc aaaaaacgta acaaccaatg cttacttgtt ctggattcca 840  
 ttgacaacc ttgtcttgg atccttgtcc ctttctgtag ttggtcaaaa cttagcggat 900  
 gctagtgtac cagttacaca tagatag 927

45

<210> 75  
 <211> 234  
 <212> DNA  
 <213> Streptococcus pneumoniae

50

<400> 75  
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 tttgaacgca gtaaagctcg cgttttgaa gctgtaatgc agcgtttgac agggatttta 180  
 gtctttttct ggctagccat tgccttagca ttgacggtat tatcaagtag ataa 234

55

<210> 76  
 <211> 1110  
 <212> DNA

&lt;213&gt; Streptococcus pneumoniae

&lt;400&gt; 76

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 ttgggtctggg gaatgggtcat aggtgttgct tatctcttac ctattttgat taatcagtta 300  
 10 tctagtttga ttatatctag tcaaaactatt tatagtcgag tacaagactt aatcatagac 360  
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 ttatcctatg ttgatattct tcaaaatata ctaaatagcg tatcaaatag tgtggggagc 480  
 gtcttgctag ctcttatcag tactgttttg attttgatta tgactccagt ttttttggtt 540  
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 gatcgcttgc atattgcagg cttattaaag aattttaaag cgacgattgc tcgctatatt 660  
 15 agtggagttt cgattgacgc aatcattata ggtgttttg cttatatttg ctatagtatt 720  
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 aaagaacgag aaagagaatt agctaagtaa 1110

&lt;210&gt; 77

&lt;211&gt; 1356

&lt;212&gt; DNA

&lt;213&gt; Streptococcus pneumoniae

&lt;400&gt; 77

30 atgtatcaag cactttatcg aaaatataga agtcaaaact tctcccagtt agttggtcaa 60  
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 cttttttctg gtcctcgtgg aacgggaaaa accagtgttg ctaaaatctt tgccaaggct 180  
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 35 gtgacggacg gtatgtttaga agatgtcatt gaaatggatg cagcttctaa taatggggta 300  
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 50 ggagcggttg aaaatgaaat tgctacgctg agacaggaag ttgcccgtct caaacaagag 1140  
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 gaaaatcctg atttaacacg tcaaaatcta attcgtttgc agaatgcatg gggagaggta 1320  
 attgaaagtc taggtgggccc ggacaagctc tgctag 1356

&lt;210&gt; 78

&lt;211&gt; 1989

&lt;212&gt; DNA

&lt;213&gt; Streptococcus pneumoniae

<400> 78  
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 gtgattgggt tactggatc gactatgatg ttgattgtga ccttgtctat ctgcgctatc 1920  
 35 ttcctcatcg cctatgtgct gattttcatg attacttcaa gaagttatcg caagattgtg 1980  
 caaatgtaa 1989

&lt;210&gt; 79

&lt;211&gt; 891

40 &lt;212&gt; DNA

<213> *Streptococcus pneumoniae*

&lt;400&gt; 79

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 45 ttagaacaag accagctcaa tcacgcctat ctcttttcag gtttcttttg aagcttggaa 120  
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 50 caagcaggga ttgaaagcca gcaacaggtc tttattatcg agcaagcggg taaaatgcat 360  
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<211> 615  
5 <212> DNA  
<213> Streptococcus pneumoniae

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15 tactcaggca agggctttga aggaaataaa ggaactttct ttagaagtat cgctcaaaaa 420  
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ggagaatacc ttctcctcgg agatgaccgc ttggttttga gcgacagccg ccacgtagggt 540  
accttcaaag caaaagatat cacaggggaa gctaaattcc gcttctggcc aatcacccgt 600  
atcggaacat tttaa 615

<210> 81  
<211> 987  
<212> DNA  
20 <213> Streptococcus pneumoniae

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30 ggtctatttg gtaaaaaaac agcccaagtg gatattgaag cgattagtga aacgactgtt 180  
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catcgtatta tttcacgtat ggatggcgtg actagttact ctgaagggtga tgagccaaat 960  
cgctatgttg ttgtagatac agaataa 987

<210> 82  
<211> 1383  
<212> DNA  
45 <213> Streptococcus pneumoniae

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cataaaaatg tggccactat cttgactgct gaaacggata atccttttgg ctatggacga 420

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 45 <213> Streptococcus pneumoniae

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- <400> 93

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25 &lt;212&gt; DNA

&lt;213&gt; Streptococcus pneumoniae

&lt;400&gt; 94

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&lt;211&gt; 750

&lt;212&gt; DNA

50 &lt;213&gt; Streptococcus pneumoniae

&lt;400&gt; 95

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 <212> DNA

<213> *Streptococcus pneumoniae*

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&lt;212&gt; DNA

<213> *Streptococcus pneumoniae*

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55 &lt;211&gt; 1446

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&lt;213&gt; Streptococcus pneumoniae

&lt;400&gt; 104

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25

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 cacgaagtgg cagccatcta tgacaaggca gtcaacttta aagaatttac tcaacagaa 600  
 10 actaatgaag ctgcggcaga tgccctttct gtcagcattg agacagacaa ggcgccttac 660  
 tatgcagctc gtatcttga caatgtgacc atcgaccaa gtccacaatg gttgcaaac 720  
 cttctcatga acgaaggaat ccgtccatc aataacgtag tggacgtgac caactacatc 780  
 ctgctctatt ttggtcaacc aatgcattgc ttgacttgg ataactttga agggactgac 840  
 atccgtgtgc gtgaagcgcg tgctggtgaa aaattggtga ccttggacgg tgaagaacgt 900  
 gacttggacg tgaatgacct agtcatcact gtcgcagaca agccagtagc ccttgcaggt 960  
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 gaccaagttc ttggtttcct tggccaagt catccagtca ctgccaaggc ttacgatatt 2040  
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 40 taa 2403  
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 <212> DNA  
 <213> Streptococcus pneumoniae  
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 50 attttaaaag gatctattcc ttttatggct gaattggtca aacatattga tacacatatt 180  
 gaaatggact tcatgatggt ttctagctac catggtggaa cagcaagtag tgggtttatc 240  
 aatattaaac aagatgtgac tcaagatata aaaggaagac atgttctatt tgtagaagat 300  
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 gcttctgtta aaattgcaac cttgttggat aaaccagaag gacgtgttgt agaaattgag 420  
 gcagactata cctgctttac tatcccaaat gagttttag taggttatgg tttagactac 480  
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<210> 114  
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 <212> PRT  
 <213> Streptococcus pneumoniae

5

<400> 114  
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10

Ile Ser Asn Leu Pro Lys Gln Phe Leu Glu Leu Gly Asp Arg Pro Ile  
 20 25 30

Leu Ile His Thr Ile Glu Lys Phe Val Leu Glu Pro Ser Ile Glu Lys  
 35 40 45

15

Ile Val Val Gly Val His Gly Asp Trp Val Leu His Ala Glu Asp Leu  
 50 55 60

Val Asp Lys Tyr Leu Pro Leu His Lys Glu Arg Ile Ile Ile Thr Lys  
 65 70 75 80

Gly Gly Ala Asp Arg Asn Thr Ser Ile Glu Asn Ile Ile Glu Ala Ile  
 85 90 95

25

Asp Ala Tyr Arg Pro Leu Thr Pro Glu Asp Ile Val Val Thr His Asp  
 100 105 110

Ser Val Arg Pro Phe Ile Thr Leu Arg Met Ile Gln Asp Ser Ile Lys  
 115 120 125

30

Leu Ala Gln Asn His Asp Ala Val Asp Thr Val Val Glu Ala Val Asp  
 130 135 140

Thr Ile Val Glu Ser Thr Asn Gly Gln Phe Ile Thr Gly Ile Pro Asn  
 145 150 155 160

35

Arg Ala His Leu Tyr Gln Gly Gln Thr Pro Gln Thr Phe Arg Cys Lys  
 165 170 175

40

Asp Phe Met Asp Leu Tyr Gly Ser Leu Ser Asp Glu Glu Lys Glu Ile  
 180 185 190

Leu Thr Asp Ala Cys Lys Ile Phe Val Ile Lys Gly Lys Asp Val Ala  
 195 200 205

45

Leu Ala Lys Gly Glu Tyr Ser Asn Leu Lys Ile Thr Thr Val Thr Asp  
 210 215 220

Leu Lys Ile Ala Lys Ser Met Ile Glu Lys Asp  
 225 230 235

50

<210> 115  
 <211> 185  
 <212> PRT  
 <213> Streptococcus pneumoniae

55

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 Asn Ala Ser Leu Leu Asp Arg Val His Val Glu Tyr Tyr Gly Val Glu  
 35 40 45  
 10 Thr Pro Leu Asn Gln Ile Ala Ser Ile Thr Ile Pro Glu Ala Arg Val  
 50 55 60  
 15 Leu Leu Val Thr Pro Phe Asp Lys Ser Ser Leu Lys Asp Ile Glu Arg  
 65 70 75 80  
 Ala Leu Asn Ala Ser Asp Leu Gly Ile Thr Pro Ala Asn Asp Gly Ser  
 85 90 95  
 20 Val Ile Arg Leu Val Ile Pro Ala Leu Thr Glu Glu Thr Arg Arg Asp  
 100 105 110  
 Leu Ala Lys Glu Val Lys Lys Val Gly Glu Asn Ala Lys Val Ala Val  
 115 120 125  
 25 Arg Asn Ile Arg Arg Asp Ala Met Asp Glu Ala Lys Lys Gln Glu Lys  
 130 135 140  
 30 Ala Gln Glu Ile Thr Glu Asp Glu Leu Lys Thr Leu Glu Lys Asp Ile  
 145 150 155 160  
 Gln Lys Val Thr Asp Asp Ala Val Lys His Ile Asp Asp Met Thr Ala  
 165 170 175  
 35 Asn Lys Glu Lys Glu Leu Leu Glu Val  
 180 185  
 40 <210> 116  
 <211> 450  
 <212> PRT  
 <213> Streptococcus pneumoniae  
 <400> 116  
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 Glu Leu Thr Pro Glu Leu Ala Phe Lys Leu Gly Arg Phe Gly Gly Tyr  
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 50 Val Leu Ser Gln His Glu Thr Glu Ala Pro Lys Val Phe Val Gly Arg  
 35 40 45  
 55 Asp Thr Arg Ile Ser Gly Glu Met Leu Glu Ser Ala Leu Val Ala Gly  
 50 55 60  
 Leu Leu Ser Val Gly Ile His Val Tyr Lys Leu Gly Val Leu Ala Thr

	65	70	75	80
	Pro Ala Val	Ala Tyr Leu Val	Glu Thr Glu Gly Ala Ser	Ala Gly Val
		85	90	95
5	Met Ile Ser	Ala Ser His Asn Pro	Ala Leu Asp Asn Gly	Ile Lys Phe
	100		105	110
10	Phe Gly Gly	Asp Gly Phe Lys Leu Asp	Asp Glu Lys Glu Ala	Glu Ile
	115		120	125
	Glu Ala Leu	Leu Asp Ala Glu Glu Asp	Thr Leu Pro Arg Pro	Ser Ala
	130		135	140
15	Glu Gly Leu	Gly Ile Leu Val Asp Tyr Pro	Glu Gly Leu Arg Lys	Tyr
	145		150	155
	Glu Gly Tyr	Arg Val Ser Thr Gly Thr	Pro Leu Asp Gly Met	Lys Val
		165	170	175
20	Ala Leu Asp	Thr Ala Asn Gly Ala Ala Ser	Thr Ser Ala Arg	Gln Ile
		180	185	190
25	Phe Ala Asp	Leu Gly Ala Gln Leu Thr Val	Ile Gly Glu Thr Pro	Asp
	195		200	205
	Gly Leu Asn	Ile Asn Leu Asn Val Gly Ser	Thr His Pro Glu Ala	Leu
	210		215	220
30	Gln Glu Val	Val Lys Glu Ser Gly Ser Ala	Ile Gly Leu Ala Phe	Asp
	225		230	235
	Gly Asp Ser	Asp Arg Leu Ile Ala Val Asp	Glu Asn Gly Asp Ile	Val
		245	250	255
35	Asp Gly Asp	Lys Ile Met Tyr Ile Ile Gly	Lys Tyr Leu Ser Glu	Lys
		260	265	270
40	Gly Gln Leu	Ala Gln Asn Thr Ile Val Thr	Thr Val Met Ser Asn	Leu
	275		280	285
	Gly Phe His	Lys Ala Leu Asn Arg Glu Gly	Ile Asn Lys Ala Val	Thr
	290		295	300
45	Ala Val Gly	Asp Arg Tyr Val Val Glu Glu	Met Arg Lys Ser Gly	Tyr
	305		310	315
	Asn Leu Gly	Gly Glu Gln Ser Gly His Val	Ile Leu Met Asp Tyr	Asn
		325	330	335
50	Thr Thr Gly	Asp Gly Gln Leu Ser Ala Val	Gln Leu Thr Lys Ile	Met
		340	345	350
55	Lys Glu Thr	Gly Lys Ser Leu Ser Glu Leu	Ala Ala Glu Val Thr	Ile
	355		360	365
	Tyr Pro Gln	Lys Leu Val Asn Ile Arg Val	Glu Asn Val Met Lys	Glu

370                      375                      380  
 Lys Ala Met Glu Val Pro Ala Ile Lys Ala Ile Ile Glu Lys Met Glu  
 385                      390                      395                      400  
 5    Glu Glu Met Ala Gly Asn Gly Arg Ile Leu Val Arg Pro Ser Gly Thr  
                                  405                      410                      415  
 10    Glu Pro Leu Leu Arg Val Met Ala Glu Ala Pro Thr Thr Glu Glu Val  
                                  420                      425                      430  
   Asp Tyr Tyr Val Asp Thr Ile Thr Asp Val Val Arg Ala Glu Ile Gly  
                                  435                      440                      445  
 15    Ile Asp  
                                  450  
 20    <210> 117  
       <211> 234  
       <212> PRT  
       <213> Streptococcus pneumoniae  
 25    <400> 117  
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       Ile Lys Phe Asn Met Thr Lys Glu Gly Tyr Glu Val Val Thr Ala Phe  
                                  20                      25                      30  
 30    Asn Gly Arg Glu Ala Leu Glu Gln Phe Glu Ala Glu Gln Pro Asp Ile  
                                  35                      40                      45  
 35    Ile Ile Leu Asp Leu Met Leu Pro Glu Ile Asp Gly Leu Glu Val Ala  
           50                      55                      60  
       Lys Thr Ile Arg Lys Thr Ser Ser Val Pro Ile Leu Met Leu Ser Ala  
           65                      70                      75                      80  
 40    Lys Asp Ser Glu Phe Asp Lys Val Ile Gly Leu Glu Leu Gly Ala Asp  
                                  85                      90                      95  
       Asp Tyr Val Thr Lys Pro Phe Ser Asn Arg Glu Leu Gln Ala Arg Val  
                                  100                      105                      110  
 45    Lys Ala Leu Leu Arg Arg Ser Gln Pro Met Pro Val Asp Gly Gln Glu  
                                  115                      120                      125  
 50    Ala Asp Ser Lys Pro Gln Pro Ile Gln Ile Gly Asp Leu Glu Ile Val  
           130                      135                      140  
       Pro Asp Ala Tyr Val Ala Lys Lys Tyr Gly Glu Glu Leu Asp Leu Thr  
           145                      150                      155                      160  
 55    His Arg Glu Phe Glu Leu Leu Tyr His Leu Ala Ser His Thr Gly Gln  
                                  165                      170                      175



Val Ile Thr Arg Glu His Leu Leu Glu Thr Val Trp Gly Tyr Asp Tyr  
 180 185 190  
 5 Phe Gly Asp Val Arg Thr Val Asp Val Thr Val Arg Arg Leu Arg Glu  
 195 200 205  
 Lys Ile Glu Asp Thr Pro Ser Arg Pro Glu Tyr Ile Leu Thr Arg Arg  
 210 215 220  
 10 Gly Val Gly Tyr Tyr Met Arg Asn Asn Ala  
 225 230  
 15 <210> 118  
 <211> 368  
 <212> PRT  
 <213> Streptococcus pneumoniae  
 <400> 118  
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 Asp Lys Ala Gly Leu Gly Phe Thr Pro Gln Ser Ala Leu Glu Lys Gly  
 20 25 30  
 25 Leu Glu Thr Gly Glu Val Tyr Cys Gln Arg Cys Phe Arg Leu Arg His  
 35 40 45  
 30 Tyr Asn Glu Ile Thr Asp Val Gln Leu Thr Asn Asp Asp Phe Leu Lys  
 50 55 60  
 Leu Leu His Glu Val Gly Asp Ser Asp Ala Leu Val Val Asn Val Ile  
 65 70 75 80  
 35 Asp Ile Phe Asp Phe Asn Gly Ser Val Ile Pro Gly Leu Pro Arg Phe  
 85 90 95  
 Val Ser Gly Asn Asp Val Leu Leu Val Gly Asn Lys Lys Asp Ile Leu  
 100 105 110  
 40 Pro Lys Ser Val Lys Ser Gly Lys Ile Ser Gln Trp Leu Met Lys Arg  
 115 120 125  
 45 Ala His Glu Glu Gly Leu Arg Pro Val Asp Val Val Leu Thr Ser Ala  
 130 135 140  
 Gln Asn Lys His Ala Ile Lys Glu Val Ile Asp Lys Ile Glu His Tyr  
 145 150 155 160  
 50 Arg Lys Gly Arg Asp Val Tyr Val Val Gly Val Thr Asn Val Gly Lys  
 165 170 175  
 Ser Thr Leu Ile Asn Ala Ile Ile Gln Glu Ile Thr Gly Asp Gln Asn  
 180 185 190  
 55 Val Ile Thr Thr Ser Arg Phe Pro Gly Thr Thr Leu Asp Lys Ile Glu  
 195 200 205

Ile Pro Leu Asp Asp Gly Ser Tyr Ile Tyr Asp Thr Pro Gly Ile Ile  
 210 215 220  
 5 His Arg His Gln Met Ala His Tyr Leu Thr Ala Lys Asn Leu Lys Tyr  
 225 230 235 240  
 Val Ser Pro Lys Lys Glu Ile Lys Pro Lys Thr Tyr Gln Leu Asn Pro  
 245 250 255  
 10 Glu Gln Thr Leu Phe Leu Gly Gly Leu Gly Arg Phe Asp Phe Ile Ala  
 260 265 270  
 Gly Glu Lys Gln Gly Phe Thr Ala Phe Phe Asp Asn Glu Leu Lys Leu  
 15 275 280 285  
 His Arg Ser Lys Leu Glu Gly Ala Ser Ala Phe Tyr Asp Lys His Leu  
 290 295 300  
 20 Gly Thr Leu Leu Thr Pro Pro Asn Ser Lys Glu Lys Glu Asp Phe Pro  
 305 310 315 320  
 Arg Leu Val Gln His Val Phe Thr Ile Lys Asp Lys Thr Asp Leu Val  
 325 330 335  
 25 Ile Ser Gly Leu Gly Trp Ile Arg Val Thr Gly Thr Ala Lys Val Ala  
 340 345 350  
 Val Trp Ala Pro Glu Gly Val Ala Val Val Thr Arg Lys Ala Ile Ile  
 30 355 360 365  
 35  
 <210> 119  
 <211> 486  
 <212> PRT  
 <213> Streptococcus pneumoniae  
 40  
 <400> 119  
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 45 Asn Met Met Gln Val Tyr Phe Asp Gln Gly Ile His Asn Lys Lys Ala  
 20 25 30  
 Val Phe Glu Val Tyr Phe Arg Gln Gln Pro Phe Lys Asn Gly Tyr Ala  
 35 40 45  
 50 Val Phe Ala Gly Leu Glu Arg Ile Val Asn Tyr Leu Glu Asp Leu Arg  
 50 55 60  
 Phe Ser Asp Ser Asp Ile Ala Tyr Leu Glu Ser Leu Gly Tyr His Gly  
 55 65 70 75 80  
 Ala Phe Leu Asp Tyr Leu Arg Asn Phe Lys Leu Glu Leu Thr Val Arg

	85	90	95
	Ser Ala Gln Glu Gly Asp Leu Val Phe Ala Asn Glu Pro Ile Val Gln		
	100	105	110
5	Val Glu Gly Pro Leu Ala Gln Cys Gln Leu Val Glu Thr Ala Leu Leu		
	115	120	125
10	Asn Ile Val Asn Tyr Gln Thr Leu Val Ala Thr Lys Ala Ala Arg Ile		
	130	135	140
	Arg Ser Val Ile Glu Asp Glu Pro Leu Met Glu Phe Gly Thr Arg Arg		
	145	150	155 160
15	Ala Gln Glu Thr Asp Ala Ala Ile Trp Gly Thr Arg Ala Ala Val Ile		
	165	170	175
	Gly Gly Ala Asn Gly Thr Ser Asn Val Arg Ala Gly Lys Leu Phe Asp		
	180	185	190
20	Ile Pro Val Leu Gly Thr His Ala His Ala Leu Val Gln Val Tyr Gly		
	195	200	205
	Asn Asp Tyr Glu Ala Phe Lys Ala Tyr Ala Ala Thr His Lys Asn Cys		
25	210	215	220
	Val Phe Leu Val Asp Thr Tyr Asp Thr Leu Arg Ile Gly Val Pro Ala		
	225	230	235 240
30	Ala Ile Gln Val Ala Arg Glu Leu Gly Asp Gln Ile Asn Phe Met Gly		
	245	250	255
	Val Arg Ile Asp Ser Gly Asp Ile Ala Tyr Ile Ser Lys Lys Val Arg		
	260	265	270
35	Gln Gln Leu Asp Glu Ala Gly Phe Thr Glu Ala Lys Ile Tyr Ala Ser		
	275	280	285
	Asn Asp Leu Asp Glu Asn Thr Ile Leu Asn Leu Lys Met Gln Lys Ala		
40	290	295	300
	Lys Ile Asp Val Trp Gly Val Gly Thr Gln Leu Ile Thr Ala Tyr Asp		
	305	310	315 320
45	Gln Pro Ala Leu Gly Ala Val Tyr Lys Ile Val Ala Ile Glu Asp Glu		
	325	330	335
	Thr Gly Gln Met Arg Asn Thr Ile Lys Leu Ser Asn Asn Ala Glu Lys		
	340	345	350
50	Val Ser Thr Pro Gly Lys Lys Gln Val Trp Arg Ile Thr Ser Arg Glu		
	355	360	365
	Lys Gly Lys Ser Glu Gly Asp Tyr Ile Thr Tyr Asp Gly Val Asp Ile		
55	370	375	380
	Ser Asp Met Thr Glu Ile Lys Met Phe His Pro Thr Tyr Thr Tyr Ile		

385                      390                      395                      400  
 Lys Lys Thr Val Arg Asn Phe Asp Ala Val Pro Leu Leu Val Asp Ile  
                                  405                      410                      415  
 5 Phe Lys Glu Gly Ile Leu Val Tyr Asn Leu Pro Ser Leu Thr Asp Ile  
                                  420                      425                      430  
 10 Gln Asp Tyr Ala Arg Lys Glu Phe Asp Lys Leu Trp Asp Glu Tyr Lys  
                                  435                      440                      445  
 Arg Val Leu Asn Pro Gln His Tyr Pro Val Asp Leu Ala Arg Asp Val  
                                  450                      455                      460  
 15 Trp Gln Asp Lys Met Asp Leu Ile Asp Lys Met Arg Lys Glu Ala Leu  
                                  465                      470                      475                      480  
 Gly Glu Gly Glu Glu Glu  
                                  485  
 20  
 <210> 120  
 <211> 283  
 <212> PRT  
 25 <213> Streptococcus pneumoniae  
 <400> 120  
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 30 Gln Val Gln Glu Asn Leu Lys Phe Val Asp Phe Val Thr Ile Leu Val  
                                  20                      25                      30  
 35 Asp Ala Arg Leu Pro Leu Ser Ser Gln Asn Pro Met Leu Thr Lys Ile  
                                  35                      40                      45  
 Val Gly Asp Lys Pro Lys Leu Leu Ile Leu Asn Lys Ala Asp Leu Ala  
   50                      55                      60  
 40 Asp Pro Ala Met Thr Lys Glu Trp Arg Gln Tyr Phe Glu Ser Gln Gly  
   65                      70                      75                      80  
 Ile Gln Thr Leu Ala Ile Asn Ser Lys Glu Gln Val Thr Val Lys Val  
                                  85                      90                      95  
 45 Val Thr Asp Ala Ala Lys Lys Leu Met Ala Asp Lys Ile Ala Arg Gln  
                                  100                      105                      110  
 50 Lys Glu Arg Gly Ile Gln Ile Glu Thr Leu Arg Thr Met Ile Ile Gly  
                                  115                      120                      125  
 Ile Pro Asn Ala Gly Lys Ser Thr Leu Met Asn Arg Leu Ala Gly Lys  
   130                      135                      140  
 55 Lys Ile Ala Val Val Gly Asn Lys Pro Gly Val Thr Lys Gly Gln Gln  
   145                      150                      155                      160

Trp Leu Lys Thr Asn Lys Asp Leu Glu Ile Leu Asp Thr Pro Gly Ile  
 165 170 175  
 5 Leu Trp Pro Lys Phe Glu Asp Glu Thr Val Ala Leu Lys Leu Ala Leu  
 180 185 190  
 Thr Gly Ala Ile Lys Asp Gln Leu Leu Pro Met Asp Glu Val Thr Ile  
 195 200 205  
 10 Phe Gly Ile Asn Tyr Phe Lys Glu His Tyr Pro Glu Lys Leu Ala Glu  
 210 215 220  
 Arg Phe Lys Gln Met Lys Ile Glu Glu Glu Pro Ser Val Ile Ile Met  
 225 230 235 240  
 15 Asp Met Thr Arg Ala Leu Gly Phe Arg Asp Asp Tyr Asp Arg Phe Tyr  
 245 250 255  
 20 Ser Leu Phe Val Lys Glu Val Arg Asp Gly Lys Leu Gly Asn Tyr Thr  
 260 265 270  
 Leu Asp Thr Leu Glu Asp Leu Asp Gly Asn Asp  
 275 280  
 25  
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 <211> 156  
 <212> PRT  
 <213> Streptococcus pneumoniae  
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 20 25 30  
 Val Asn Arg Thr Phe Lys Ser Gln Asn Gly Glu Arg Glu Ala Asp Phe  
 35 40 45  
 40 Ile Asn Val Val Met Trp Arg Gln Gln Ala Glu Asn Leu Ala Asn Trp  
 50 55 60  
 Ala Lys Lys Gly Ser Leu Ile Gly Val Thr Gly Arg Ile Gln Thr Arg  
 45 65 70 75 80  
 Ser Tyr Asp Asn Gln Gln Gly Gln Arg Val Tyr Val Thr Glu Val Val  
 85 90 95  
 50 Ala Glu Asn Phe Gln Met Leu Glu Ser Arg Ser Val Arg Glu Gly His  
 100 105 110  
 Thr Gly Gly Ala Tyr Ser Ala Pro Thr Ala Asn Tyr Ser Ala Pro Thr  
 115 120 125  
 55 Asn Ser Val Pro Asp Phe Ser Arg Asn Glu Asn Pro Phe Gly Ala Thr  
 130 135 140

Asn Pro Leu Asp Ile Ser Asp Asp Asp Leu Pro Phe  
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5  
 <210> 122  
 <211> 324  
 <212> PRT  
 <213> Streptococcus pneumoniae

10  
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 20 25 30

Ser Lys Ala Gly Gly Leu Gly Ile Ile Gly Gly Gly Asn Ala Pro Lys  
 35 40 45

20 Glu Val Val Lys Ala Asn Ile Asp Lys Ile Lys Ser Leu Thr Asp Lys  
 50 55 60

25 Pro Phe Gly Val Asn Ile Met Leu Leu Ser Pro Phe Val Glu Asp Ile  
 65 70 75 80

Val Asp Leu Val Ile Glu Glu Gly Val Lys Val Val Thr Thr Gly Ala  
 85 90 95

30 Gly Asn Pro Ser Lys Tyr Met Glu Arg Phe His Glu Ala Gly Ile Ile  
 100 105 110

Val Ile Pro Val Val Pro Ser Val Ala Leu Ala Lys Arg Met Glu Lys  
 115 120 125

35 Ile Gly Ala Asp Ala Val Ile Ala Glu Gly Met Glu Ala Gly Gly His  
 130 135 140

40 Ile Gly Lys Leu Thr Thr Met Thr Leu Val Arg Gln Val Ala Thr Ala  
 145 150 155 160

Ile Ser Ile Pro Val Ile Ala Ala Gly Gly Ile Ala Asp Gly Glu Gly  
 165 170 175

45 Ala Ala Ala Gly Phe Met Leu Gly Ala Glu Ala Val Gln Val Gly Thr  
 180 185 190

Arg Phe Val Val Ala Lys Glu Ser Asn Ala His Pro Asn Tyr Lys Glu  
 195 200 205

50 Lys Ile Leu Lys Ala Arg Asp Ile Asp Thr Thr Ile Ser Ala Gln His  
 210 215 220

55 Phe Gly His Ala Val Arg Ala Ile Lys Asn Gln Leu Thr Arg Asp Phe  
 225 230 235 240

Glu Leu Ala Glu Lys Asp Ala Phe Lys Gln Glu Asp Pro Asp Leu Glu

245                      250                      255  
 Ile Phe Glu Gln Met Gly Ala Gly Ala Leu Ala Lys Ala Val Val His  
                          260                      265                      270  
 5 Gly Asp Val Glu Gly Gly Ser Val Met Ala Gly Gln Ile Ala Gly Leu  
                          275                      280                      285  
 10 Val Ser Lys Glu Glu Thr Ala Glu Glu Ile Leu Lys Asp Leu Tyr Tyr  
                          290                      295                      300  
 Gly Ala Ala Lys Lys Ile Gln Glu Glu Ala Ser Arg Trp Thr Gly Val  
 305                      310                      315                      320  
 15 Val Arg Asn Asp  
  
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     <211> 140  
     <212> PRT  
     <213> Streptococcus pneumoniae  
  
 25 <400> 123  
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                          20                      25                      30  
 30 Ala Ile Lys Asn Val Thr Ile Asn Glu Pro Phe Phe Asn Gly His Phe  
                          35                      40                      45  
 35 Pro Gln Tyr Pro Val Met Pro Gly Val Leu Ile Met Glu Ala Leu Ala  
                          50                      55                      60  
     Gln Thr Ala Gly Val Leu Glu Leu Ser Lys Pro Glu Asn Lys Gly Lys  
         65                      70                      75                      80  
 40 Leu Val Phe Tyr Ala Gly Met Asp Lys Val Lys Phe Lys Lys Gln Val  
                          85                      90                      95  
     Val Pro Gly Asp Gln Leu Val Met Thr Ala Thr Phe Val Lys Arg Arg  
                          100                      105                      110  
 45 Gly Thr Ile Ala Val Val Glu Ala Lys Ala Glu Val Asp Gly Lys Leu  
                          115                      120                      125  
 50 Ala Ala Ser Gly Thr Leu Thr Phe Ala Ile Gly Asn  
                          130                      135                      140  
  
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     <211> 340  
     <212> PRT  
     <213> Streptococcus pneumoniae

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 5 Lys Tyr Gln Glu Glu Ala Ile Asp Gln Glu Asn His Ile Leu Ile Arg  
 20 25 30  
 Pro Asn Tyr Met Ala Val Cys His Ala Asp Gln Arg Tyr Tyr Gln Gly  
 35 40 45  
 10 Lys Arg Asp Pro Lys Ile Leu Asn Lys Lys Leu Pro Met Ala Met Ile  
 50 55 60  
 15 His Glu Ser Cys Gly Ile Val Ile Ser Asp Pro Ser Gly Thr Tyr Glu  
 65 70 75 80  
 Val Gly Gln Lys Val Val Met Ile Pro Asn Gln Ser Pro Met Gln Ser  
 85 90 95  
 20 Asp Glu Glu Phe Tyr Glu Asn Tyr Met Thr Gly Thr His Phe Leu Ser  
 100 105 110  
 Ser Gly Phe Asp Gly Phe Met Arg Glu Phe Val Ser Leu Pro Lys Asp  
 115 120 125  
 25 Arg Val Val Ala Tyr Asp Ala Ile Glu Asp Thr Val Ala Ala Ile Thr  
 130 135 140  
 30 Glu Phe Val Ser Val Gly Met His Ala Met Asn Arg Leu Leu Thr Leu  
 145 150 155 160  
 Ala His Ser Lys Arg Glu Arg Ile Pro Val Ile Gly Asp Gly Ser Leu  
 165 170 175  
 35 Ala Phe Val Val Ala Asn Ile Ile Asn Tyr Thr Leu Pro Glu Ala Glu  
 180 185 190  
 Ile Val Val Ile Gly Arg His Trp Glu Lys Leu Glu Leu Phe Ser Phe  
 195 200 205  
 40 Ala Lys Glu Cys Tyr Ile Thr Asp Asn Ile Pro Glu Glu Leu Ala Phe  
 210 215 220  
 45 Asp His Ala Phe Glu Cys Cys Gly Gly Asp Gly Thr Gly Pro Ala Ile  
 225 230 235 240  
 Asn Asp Leu Ile Arg Tyr Ile Arg Pro Gln Gly Thr Ile Leu Met Met  
 245 250 255  
 50 Gly Val Ser Glu Tyr Lys Val Asn Leu Asn Thr Arg Asp Ala Leu Glu  
 260 265 270  
 Lys Gly Leu Leu Leu Val Gly Ser Ser Arg Ser Gly Arg Ile Asp Phe  
 275 280 285  
 55 Glu Asn Ala Ile Gln Met Met Lys Val Lys Lys Phe Ala Asn Arg Leu  
 290 295 300



Lys Asn Ile Leu Tyr Leu Glu Glu Pro Val Arg Glu Ile Lys Asp Ile  
 305 310 315 320  
 5 His Arg Val Phe Ala Thr Asp Leu Asn Thr Ala Phe Lys Thr Val Phe  
 325 330 335  
 Lys Trp Glu Val  
 340  
 10  
 <210> 125  
 <211> 447  
 <212> PRT  
 15 <213> Streptococcus pneumoniae  
 <400> 125  
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 1 5 10 15  
 20 Phe Val Leu Ser Arg Leu Gly Arg Gly Ser Thr Leu Pro Gly Lys Val  
 20 25 30  
 25 Ala Leu Gln Phe Asp Lys Asp Ile Leu Gln Asn Leu Ala Lys Asn Tyr  
 35 40 45  
 Glu Ile Val Val Val Thr Gly Thr Asn Gly Lys Thr Leu Thr Thr Ala  
 50 55 60  
 30 Leu Thr Val Gly Ile Leu Lys Glu Val Tyr Gly Gln Val Leu Thr Asn  
 65 70 75 80  
 Pro Ser Gly Ala Asn Met Ile Thr Gly Ile Ala Thr Thr Phe Leu Thr  
 85 90 95  
 35 Ala Lys Ser Ser Lys Thr Gly Lys Asn Ile Ala Val Leu Glu Ile Asp  
 100 105 110  
 40 Glu Ala Ser Leu Ser Arg Ile Cys Asp Tyr Ile Gln Pro Ser Leu Phe  
 115 120 125  
 Val Ile Thr Asn Ile Phe Arg Asp Gln Met Asp Arg Phe Gly Glu Ile  
 130 135 140  
 45 Tyr Thr Thr Tyr Asn Met Ile Leu Asp Ala Ile Arg Lys Val Pro Thr  
 145 150 155 160  
 Ala Thr Val Leu Leu Asn Gly Asp Ser Pro Leu Phe Tyr Lys Pro Thr  
 165 170 175  
 50 Ile Pro Asn Pro Ile Glu Tyr Phe Gly Phe Asp Leu Glu Lys Gly Pro  
 180 185 190  
 55 Ala Gln Leu Ala His Tyr Asn Thr Glu Gly Ile Leu Cys Pro Asp Cys  
 195 200 205  
 Gln Gly Ile Leu Lys Tyr Glu His Asn Thr Tyr Ala Asn Leu Gly Ala

210                      215                      220  
 Tyr Ile Cys Glu Gly Cys Gly Cys Lys Arg Pro Asp Leu Asp Tyr Arg  
 225                      230                      235                      240  
 5    Leu Thr Lys Leu Val Glu Leu Thr Asn Asn Arg Ser Arg Phe Val Ile  
                                  245                      250                      255  
 10    Asp Gly Gln Glu Tyr Gly Ile Gln Ile Gly Gly Leu Tyr Asn Ile Tyr  
                                  260                      265                      270  
       Asn Ala Leu Ala Ala Val Ala Ile Ala Arg Phe Leu Gly Ala Asp Ser  
                                  275                      280                      285  
 15    Gln Leu Ile Lys Gln Gly Phe Asp Lys Ser Arg Ala Val Phe Gly Arg  
                                  290                      295                      300  
       Gln Glu Thr Phe His Ile Gly Asp Lys Glu Cys Thr Leu Val Leu Ile  
                                  305                      310                      315                      320  
 20    Lys Asn Pro Val Gly Ala Thr Gln Ala Ile Glu Met Ile Lys Leu Ala  
                                  325                      330                      335  
 25    Pro Tyr Pro Phe Ser Leu Ser Val Leu Leu Asn Ala Asn Tyr Ala Asp  
                                  340                      345                      350  
       Gly Ile Asp Thr Ser Trp Ile Trp Asp Ala Asp Phe Glu Gln Ile Thr  
                                  355                      360                      365  
 30    Asp Met Asp Ile Pro Glu Ile Asn Ala Gly Gly Val Arg His Ser Glu  
                                  370                      375                      380  
       Ile Ala Arg Arg Leu Arg Val Thr Gly Tyr Pro Ala Glu Lys Ile Thr  
                                  385                      390                      395                      400  
 35    Glu Thr Ser Asn Leu Glu Gln Val Leu Lys Thr Ile Glu Asn Gln Asp  
                                  405                      410                      415  
 40    Cys Lys His Ala Tyr Ile Leu Ala Thr Tyr Thr Ala Met Leu Glu Phe  
                                  420                      425                      430  
       Arg Glu Leu Leu Ala Ser Arg Gln Ile Val Arg Lys Glu Met Asn  
                                  435                      440                      445  
 45    <210> 126  
       <211> 260  
       <212> PRT  
       <213> Streptococcus pneumoniae  
 50    <400> 126  
       Met Val Tyr Thr Ser Leu Ser Ser Lys Asp Gly Asn Tyr Pro Tyr Gln  
                                  1                      5                      10                      15  
 55    Leu Asn Ile Ala His Leu Tyr Gly Asn Leu Met Asn Thr Tyr Gly Asp  
                                  20                      25                      30

Asn Gly Asn Ile Leu Met Leu Lys Tyr Val Ala Glu Lys Leu Gly Ala  
                   35                                  40                                  45  
 5 His Val Thr Val Asp Ile Val Ser Leu His Asp Asp Phe Asp Glu Asn  
                   50                                  55                                  60  
 His Tyr Asp Ile Ala Phe Phe Gly Gly Gly Gln Asp Phe Glu Gln Ser  
                   65                                  70                                  75                                  80  
 10 Ile Ile Ala Asp Asp Leu Pro Ala Lys Lys Glu Ser Ile Asp Asn Tyr  
                                   85                                  90                                  95  
 Ile Gln Asn Asp Gly Val Val Leu Ala Ile Cys Gly Gly Phe Gln Leu  
                                   100                                  105                                  110  
 15 Leu Gly Gln Tyr Tyr Val Glu Ala Ser Gly Lys Arg Ile Glu Gly Leu  
                                   115                                  120                                  125  
 Gly Val Met Gly His Tyr Thr Leu Asn Gln Thr Asn Asn Arg Phe Ile  
                   130                                  135                                  140  
 Gly Asp Ile Lys Ile His Asn Glu Asp Phe Asp Glu Thr Tyr Tyr Gly  
                   145                                  150                                  155                                  160  
 25 Phe Glu Asn His Gln Gly Arg Thr Phe Leu Ser Asp Asp Gln Lys Pro  
                                   165                                  170                                  175  
 Leu Gly Gln Val Val Tyr Gly Asn Gly Asn Asn Glu Glu Lys Val Gly  
                                   180                                  185                                  190  
 30 Glu Gly Val His Tyr Lys Asn Val Phe Gly Ser Tyr Phe His Gly Pro  
                                   195                                  200                                  205  
 Ile Leu Ser Arg Asn Ala Asn Leu Ala Tyr Arg Leu Val Thr Thr Ala  
                   210                                  215                                  220  
 Leu Lys Lys Lys Tyr Gly Gln Asp Ile Gln Leu Pro Ala Tyr Glu Asp  
                   225                                  230                                  235                                  240  
 40 Ile Leu Ser Gln Glu Ile Ala Glu Glu Tyr Ser Asp Val Lys Ser Lys  
                                   245                                  250                                  255  
 Ala Asp Phe Ser  
                                   260  
 45  
 <210> 127  
 <211> 223  
 <212> PRT  
 50 <213> Streptococcus pneumoniae  
 <400> 127  
 Met Asn Val Lys Glu Asn Thr Glu Leu Val Phe Arg Glu Val Ala Glu  
                   1                                  5                                  10                                  15  
 55 Ala Ser Leu Ser Ala Asn Arg Glu Ser Gly Ser Val Ser Val Ile Ala  
                                   20                                  25                                  30

Val Thr Lys Tyr Val Asp Val Pro Thr Ala Glu Ala Leu Leu Pro Leu  
                   35                                  40                                  45

5 Gly Val His His Ile Gly Glu Asn Arg Val Asp Lys Phe Leu Glu Lys  
                   50                                  55                                  60

Tyr Glu Ala Leu Lys Asp Arg Asp Val Thr Trp His Leu Ile Gly Thr  
                   65                                  70                                  75                                  80

10 Leu Gln Arg Arg Lys Val Lys Asp Val Ile Gln Tyr Val Asp Tyr Phe  
                                   85                                  90                                  95

15 His Ala Leu Asp Ser Val Lys Leu Ala Gly Glu Ile Gln Lys Arg Ser  
                                   100                                  105                                  110

Asp Arg Val Ile Lys Cys Phe Leu Gln Val Asn Ile Ser Lys Glu Glu  
                   115                                  120                                  125

20 Ser Lys His Gly Phe Ser Arg Glu Glu Leu Leu Glu Ile Leu Pro Glu  
                   130                                  135                                  140

Leu Ala Gly Leu Asp Lys Ile Glu Tyr Val Gly Leu Met Thr Met Ala  
                   145                                  150                                  155                                  160

25 Pro Phe Glu Ala Ser Ser Glu Gln Leu Lys Glu Ile Phe Lys Ala Ala  
                                   165                                  170                                  175

30 Gln Asp Leu Gln Arg Glu Ile Gln Glu Lys Gln Ile Pro Asn Ile Pro  
                                   180                                  185                                  190

Met Thr Glu Leu Ser Met Gly Met Ser Arg Asp Tyr Lys Glu Ala Ile  
                   195                                  200                                  205

35 Gln Phe Gly Ser Thr Phe Val Arg Ile Gly Thr Ser Phe Phe Lys  
                   210                                  215                                  220

<210> 128  
 40 <211> 279  
 <212> PRT  
 <213> Streptococcus pneumoniae

<400> 128

45 Met Gly Ile Ala Leu Glu Asn Val Asn Phe Thr Tyr Gln Glu Gly Thr  
                   1                                  5                                  10                                  15

Pro Leu Ala Ser Ala Ala Leu Ser Asp Val Ser Leu Thr Ile Glu Asp  
                                   20                                  25                                  30

50 Gly Ser Tyr Thr Ala Leu Ile Gly His Thr Gly Ser Gly Lys Ser Thr  
                   35                                  40                                  45

55 Ile Leu Gln Leu Leu Asn Gly Leu Leu Val Pro Ser Gln Gly Ser Val  
                   50                                  55                                  60

Arg Val Phe Asp Thr Leu Ile Thr Ser Thr Ser Lys Asn Lys Asp Ile

65 70 75 80

Arg Gln Ile Arg Lys Gln Val Gly Leu Val Phe Gln Phe Ala Glu Asn  
85 90 95

5 Gln Ile Phe Glu Glu Thr Val Leu Lys Asp Val Ala Phe Gly Pro Gln  
100 105 110

10 Asn Phe Gly Val Ser Glu Glu Asp Ala Val Lys Thr Ala Arg Glu Lys  
115 120 125

Leu Ala Leu Val Gly Ile Asp Glu Ser Leu Phe Asp Arg Ser Pro Phe  
130 135 140

15 Glu Leu Ser Gly Gly Gln Met Arg Arg Val Ala Ile Ala Gly Ile Leu  
145 150 155 160

Ala Met Glu Pro Ala Ile Leu Val Leu Asp Glu Pro Thr Ala Gly Leu  
165 170 175

20 Asp Pro Leu Gly Arg Lys Glu Leu Met Thr Leu Phe Lys Lys Leu His  
180 185 190

25 Gln Ser Gly Met Thr Ile Val Leu Val Thr His Leu Met Asp Asp Val  
195 200 205

Ala Glu Tyr Ala Asn Gln Val Tyr Val Met Glu Lys Gly Arg Leu Val  
210 215 220

30 Lys Gly Gly Lys Pro Ser Asp Val Phe Gln Asp Val Val Phe Met Glu  
225 230 235 240

Glu Val Gln Leu Gly Val Pro Lys Ile Thr Ala Phe Cys Lys Arg Leu  
245 250 255

35 Ala Asp Arg Gly Val Ser Phe Lys Arg Leu Pro Val Lys Ile Glu Glu  
260 265 270

40 Phe Lys Glu Ser Leu Asn Gly  
275

<210> 129  
<211> 309  
45 <212> PRT  
<213> Streptococcus pneumoniae

<400> 129

50 Met Asp Ile Gln Phe Leu Gly Thr Gly Ala Gly Gln Pro Ser Lys Ala  
1 5 10 15

Arg Asn Val Ser Ser Leu Ala Leu Lys Leu Leu Asp Glu Ile Asn Glu  
20 25 30

55 Val Trp Leu Phe Asp Cys Gly Glu Gly Thr Gln Asn Arg Ile Leu Glu  
35 40 45

Thr Thr Ile Arg Pro Arg Lys Val Ser Lys Ile Phe Ile Thr His Leu  
 50 55 60  
 5 His Gly Asp His Ile Phe Gly Leu Pro Gly Phe Leu Ser Ser Arg Ala  
 65 70 75 80  
 Phe Gln Ala Asn Glu Glu Gln Thr Asp Leu Glu Ile Tyr Gly Pro Gln  
 85 90 95  
 10 Gly Ile Lys Ser Phe Val Leu Thr Ser Leu Arg Val Ser Gly Ser Arg  
 100 105 110  
 Leu Pro Tyr Arg Ile His Phe His Glu Phe Asp Gln Asp Ser Leu Gly  
 115 120 125  
 15 Lys Ile Leu Glu Ile Asp Lys Phe Thr Val Tyr Ala Glu Glu Leu Asp  
 130 135 140  
 20 His Thr Ile Phe Cys Val Gly Tyr Arg Val Met Gln Lys Asp Leu Glu  
 145 150 155 160  
 Gly Thr Leu Asp Ala Glu Lys Leu Lys Ala Ala Gly Val Pro Phe Gly  
 165 170 175  
 25 Pro Leu Phe Gly Lys Ile Lys Asn Gly Gln Asp Leu Val Leu Glu Asp  
 180 185 190  
 Gly Thr Glu Ile Lys Ala Ala Asp Tyr Ile Ser Ala Pro Arg Pro Gly  
 195 200 205  
 30 Lys Ile Ile Thr Ile Leu Gly Asp Thr Arg Lys Thr Asp Ala Ser Val  
 210 215 220  
 35 Arg Leu Ala Val Asn Ala Asp Val Leu Val His Glu Ser Thr Tyr Gly  
 225 230 235 240  
 Lys Gly Asp Glu Lys Ile Ala Arg Asn His Gly His Ser Thr Asn Met  
 245 250 255  
 40 Gln Ala Ala Gln Val Ala Val Glu Ala Gly Ala Lys Arg Leu Leu Leu  
 260 265 270  
 Asn His Ile Ser Ala Arg Phe Leu Ser Lys Asp Ile Ser Lys Leu Lys  
 275 280 285  
 45 Lys Asp Ala Ala Thr Ile Phe Glu Asn Val His Val Val Lys Asp Leu  
 290 295 300  
 50 Glu Glu Val Glu Ile  
 305  
 <210> 130  
 <211> 553  
 55 <212> PRT  
 <213> Streptococcus pneumoniae

<400> 130  
 Met Ser Asn Ile Ser Leu Thr Thr Leu Gly Gly Val Arg Glu Asn Gly  
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 5 Lys Asn Met Tyr Ile Ala Glu Ile Gly Glu Ser Ile Phe Val Leu Asn  
 20 25 30  
 Val Gly Leu Lys Tyr Pro Glu Asn Glu Gln Leu Gly Val Asp Val Val  
 35 40 45  
 10 Ile Pro Asn Met Asp Tyr Leu Phe Glu Asn Ser Asp Arg Ile Ala Gly  
 50 55 60  
 15 Val Phe Leu Thr His Gly His Ala Asp Ala Ile Gly Ala Leu Pro Tyr  
 65 70 75 80  
 Leu Leu Ala Glu Ala Lys Val Pro Val Phe Gly Ser Glu Leu Thr Ile  
 85 90 95  
 20 Glu Leu Ala Lys Leu Phe Val Lys Gly Asn Asp Ala Val Lys Lys Phe  
 100 105 110  
 Asn Asp Phe His Val Ile Asp Glu Asn Thr Glu Ile Asp Phe Gly Gly  
 115 120 125  
 25 Thr Val Val Ser Phe Phe Pro Thr Thr Tyr Ser Val Pro Glu Ser Leu  
 130 135 140  
 Gly Ile Val Leu Lys Thr Ser Glu Gly Ser Ile Val Tyr Thr Gly Asp  
 145 150 155 160  
 Phe Lys Phe Asp Gln Thr Ala Ser Glu Ser Tyr Ala Thr Asp Phe Ala  
 165 170 175  
 35 Arg Leu Ala Glu Ile Gly Arg Asp Gly Val Leu Ala Leu Leu Ser Asp  
 180 185 190  
 Ser Ala Asn Ala Asp Ser Asn Ile Gln Val Ala Ser Glu Ser Glu Val  
 195 200 205  
 40 Arg Asp Glu Ile Thr Gln Thr Ile Ala Asp Trp Glu Gly Arg Ile Ile  
 210 215 220  
 Val Ala Ala Val Ser Ser Asn Leu Ser Arg Ile Gln Gln Ile Phe Asp  
 225 230 235 240  
 Ala Ala Asp Lys Thr Gly Arg Arg Ile Val Leu Thr Gly Phe Asp Ile  
 245 250 255  
 50 Glu Asn Ile Val Arg Thr Ala Ile Arg Leu Lys Lys Leu Ser Leu Ala  
 260 265 270  
 Asn Glu Ile Leu Leu Ile Lys Pro Lys Asp Met Ser Arg Phe Glu Asp  
 275 280 285  
 55 His Glu Leu Ile Ile Leu Glu Thr Gly Arg Met Gly Glu Pro Ile Asn  
 290 295 300

Gly Leu Arg Lys Met Ser Ile Gly Arg His Arg Tyr Val Glu Ile Lys  
 305 310 315 320  
 5 Asp Gly Asp Leu Val Tyr Ile Ala Thr Ala Pro Ser Ile Ala Lys Glu  
 325 330 335  
 Ala Phe Val Ala Arg Val Glu Asn Met Ile Tyr Gln Ala Gly Gly Val  
 340 345 350  
 10 Val Lys Leu Ile Thr Gln Ser Leu His Val Ser Gly His Gly Asn Val  
 355 360 365  
 Arg Asp Leu Gln Leu Met Ile Asn Leu Leu Gln Pro Lys Tyr Leu Phe  
 370 375 380  
 15 Pro Val Gln Gly Glu Tyr Arg Glu Leu Asp Ala His Ala Lys Ala Ala  
 385 390 395 400  
 20 Met Ala Val Gly Met Leu Pro Glu Arg Ile Phe Ile Pro Lys Lys Gly  
 405 410 415  
 Thr Thr Met Ala Tyr Glu Asn Gly Asp Phe Val Pro Ala Gly Ser Val  
 420 425 430  
 25 Ser Ala Gly Asp Ile Leu Ile Asp Gly Asn Ala Ile Gly Asp Val Gly  
 435 440 445  
 Asn Val Val Leu Arg Asp Arg Lys Val Leu Ser Glu Asp Gly Ile Phe  
 450 455 460  
 30 Ile Val Ala Ile Thr Val Asn Arg Arg Glu Lys Lys Ile Val Ala Arg  
 465 470 475 480  
 35 Ala Arg Val His Thr Arg Gly Phe Val Tyr Leu Lys Lys Ser Arg Asp  
 485 490 495  
 Ile Leu Arg Glu Ser Ser Glu Leu Ile Asn Gln Thr Val Glu Asp Tyr  
 500 505 510  
 40 Leu Gln Gly Asp Asp Phe Asp Trp Ala Asp Leu Lys Gly Lys Val Arg  
 515 520 525  
 Asp Asn Leu Thr Lys Tyr Leu Phe Asp Gln Thr Lys Arg Arg Pro Ala  
 530 535 540  
 45 Ile Leu Pro Val Val Met Glu Ala Lys  
 545 550  
 50  
 <210> 131  
 <211> 316  
 <212> PRT  
 <213> Streptococcus pneumoniae  
 55  
 <400> 131  
 Met Thr Lys Glu Phe His His Val Thr Val Leu Leu His Glu Thr Ile



1                      5                      10                      15  
 Asp Met Leu Asp Val Lys Pro Asp Gly Ile Tyr Val Asp Ala Thr Leu  
                          20                      25                      30  
 5 Gly Gly Ala Gly His Ser Glu Tyr Leu Leu Ser Lys Leu Ser Glu Lys  
                          35                      40                      45  
 10 Gly His Leu Tyr Ala Phe Asp Gln Asp Gln Asn Ala Ile Asp Asn Ala  
                          50                      55                      60  
 Gln Lys Arg Leu Ala Pro Tyr Ile Glu Lys Gly Val Val Thr Phe Ile  
                          65                      70                      75                      80  
 15 Lys Asp Asn Phe Arg His Leu Gln Ala Arg Leu Arg Glu Ala Gly Val  
                          85                      90                      95  
 Gln Glu Ile Asp Gly Ile Cys Tyr Asp Leu Gly Val Ser Ser Pro Gln  
                          100                      105                      110  
 20 Leu Asp Gln Arg Glu Arg Gly Phe Ser Tyr Lys Lys Asp Ala Pro Leu  
                          115                      120                      125  
 25 Asp Met Arg Met Asn Gln Asp Ala Ser Leu Thr Ala Tyr Glu Val Val  
                          130                      135                      140  
 Asn His Tyr Asp Tyr His Asp Leu Val Arg Ile Phe Phe Lys Tyr Gly  
                          145                      150                      155                      160  
 30 Glu Asp Lys Phe Ser Lys Gln Ile Ala Arg Lys Ile Glu Gln Ala Arg  
                          165                      170                      175  
 Glu Val Lys Pro Ile Glu Thr Thr Thr Glu Leu Ala Glu Ile Ile Lys  
                          180                      185                      190  
 35 Leu Val Lys Pro Ala Lys Glu Leu Lys Lys Lys Gly His Pro Ala Lys  
                          195                      200                      205  
 40 Gln Ile Phe Gln Ala Ile Arg Ile Glu Val Asn Asp Glu Leu Gly Ala  
                          210                      215                      220  
 Ala Asp Glu Ser Ile Gln Gln Ala Met Asp Met Leu Ala Leu Asp Gly  
                          225                      230                      235                      240  
 45 Arg Ile Ser Val Ile Thr Phe His Ser Leu Glu Asp Arg Leu Thr Lys  
                          245                      250                      255  
 Gln Leu Phe Lys Glu Ala Ser Thr Val Glu Val Pro Lys Gly Leu Pro  
                          260                      265                      270  
 50 Phe Ile Pro Asp Asp Leu Lys Pro Lys Met Glu Leu Val Ser Arg Lys  
                          275                      280                      285  
 55 Pro Ile Leu Pro Ser Ala Glu Glu Leu Glu Ala Asn Asn Arg Ser His  
                          290                      295                      300  
 Ser Ala Lys Leu Arg Val Val Arg Lys Ile His Lys

70

Gly Leu Asp Tyr Val Asp Gln Lys Ile Leu Arg Thr Met Ile Glu Met  
 260 265 270  
 5 Tyr Ser Gly Gly Pro Val Gly Leu Gly Thr Leu Ser Val Asn Ile Ala  
 275 280 285  
 Glu Glu Arg Glu Thr Val Glu Asp Met Tyr Glu Pro Tyr Leu Ile Gln  
 290 295 300  
 10 Lys Gly Phe Ile Met Arg Thr Arg Ser Gly Arg Val Ala Thr Ala Lys  
 305 310 315 320  
 Ala Tyr Glu His Leu Gly Tyr Glu Tyr Ser Glu Lys  
 325 330  
 15  
 <210> 133  
 <211> 436  
 <212> PRT  
 20 <213> Streptococcus pneumoniae  
 <400> 133  
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 25 Gly Gly Asp Gly Met Val Ala Phe Arg Arg Glu Lys Tyr Val Pro Asn  
 20 25 30  
 Gly Gly Pro Trp Gly Gly Asp Gly Gly Arg Gly Gly Asn Val Val Phe  
 30 35 40 45  
 Val Val Asp Glu Gly Leu Arg Thr Leu Met Asp Phe Arg Tyr Asn Arg  
 50 55 60  
 35 His Phe Lys Ala Asp Ser Gly Glu Lys Gly Met Thr Lys Gly Met His  
 65 70 75 80  
 Gly Arg Gly Ala Glu Asp Leu Arg Val Arg Val Ser Gln Gly Thr Thr  
 85 90 95  
 40 Val Arg Asp Ala Glu Thr Gly Lys Val Leu Thr Asp Leu Ile Lys His  
 100 105 110  
 Gly Gln Glu Phe Ile Val Ala His Gly Gly Arg Gly Gly Arg Gly Asn  
 115 120 125  
 45 Ile Arg Phe Ala Thr Pro Lys Asn Pro Ala Pro Glu Ile Ser Glu Asn  
 130 135 140  
 50 Gly Glu Pro Gly Gln Glu Arg Glu Leu Gln Leu Glu Leu Lys Ile Leu  
 145 150 155 160  
 Ala Asp Val Gly Leu Val Gly Phe Pro Ser Val Gly Lys Ser Thr Leu  
 165 170 175  
 55 Leu Ser Val Ile Thr Ser Ala Lys Pro Lys Ile Gly Ala Tyr His Phe  
 180 185 190

Thr Thr Ile Val Pro Asn Leu Gly Met Val Arg Thr Gln Ser Gly Glu  
 195 200 205  
 5 Ser Phe Ala Val Ala Asp Leu Pro Gly Leu Ile Glu Gly Ala Ser Gln  
 210 215 220  
 Gly Val Gly Leu Gly Thr Gln Phe Leu Arg His Ile Glu Arg Thr Arg  
 225 230 235 240  
 10 Val Ile Leu His Ile Ile Asp Met Ser Ala Ser Glu Gly Arg Asp Pro  
 245 250 255  
 Tyr Glu Asp Tyr Leu Ala Ile Asn Lys Glu Leu Glu Ser Tyr Asn Leu  
 15 260 265 270  
 Arg Leu Met Glu Arg Pro Gln Ile Ile Val Ala Asn Lys Met Asp Met  
 275 280 285  
 20 Pro Glu Ser Gln Glu Asn Leu Glu Glu Phe Lys Lys Lys Leu Ala Glu  
 290 295 300  
 Asn Tyr Asp Glu Phe Glu Glu Leu Pro Ala Ile Phe Pro Ile Ser Gly  
 305 310 315 320  
 25 Leu Thr Lys Gln Gly Leu Ala Thr Leu Leu Asp Ala Thr Ala Glu Leu  
 325 330 335  
 Leu Asp Lys Thr Pro Glu Phe Leu Leu Tyr Asp Glu Ser Asp Met Glu  
 30 340 345 350  
 Glu Glu Ala Tyr Tyr Gly Phe Asp Glu Glu Glu Lys Ala Phe Glu Ile  
 355 360 365  
 35 Ser Arg Asp Asp Asp Ala Thr Trp Val Leu Ser Gly Glu Lys Leu Met  
 370 375 380  
 Lys Leu Phe Asn Met Thr Asn Phe Asp Arg Asp Glu Ser Val Met Lys  
 385 390 395 400  
 40 Phe Ala Arg Gln Leu Arg Gly Met Gly Val Asp Glu Ala Leu Arg Ala  
 405 410 415  
 Arg Gly Ala Lys Asp Gly Asp Leu Val Arg Ile Gly Lys Phe Glu Phe  
 45 420 425 430  
 Glu Phe Val Asp  
 435  
 50  
 <210> 134  
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 55  
 <400> 134  
 Met Asn Tyr Phe Asn Val Gly Lys Ile Val Asn Thr Gln Gly Leu Gln

1                      5                      10                      15  
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                                  20                      25                      30  
 5 Lys Lys Gly Ala Glu Leu Ala Leu Phe Asp Glu Lys Asp Gln Phe Val  
                                  35                      40                      45  
 10 Gln Thr Val Thr Ile Ala Ser His Arg Lys Gln Lys Asn Phe Asp Ile  
                                  50                      55                      60  
 Ile Lys Phe Lys Asp Met Tyr His Ile Asn Thr Ile Glu Lys Tyr Lys  
                                  65                      70                      75                      80  
 15 Gly Tyr Ser Leu Lys Val Ala Glu Glu Asp Leu Asn Asp Leu Asp Asp  
    85                      90                      95  
 Gly Glu Phe Tyr Tyr His Glu Ile Ile Gly Leu Glu Val Tyr Glu Gly  
                                  100                      105                      110  
 20 Asp Ser Leu Val Gly Thr Ile Lys Glu Ile Leu Gln Pro Gly Ala Asn  
                                  115                      120                      125  
 25 Asp Val Trp Val Val Lys Arg Lys Gly Lys Arg Asp Leu Leu Leu Pro  
                                  130                      135                      140  
 Tyr Ile Pro Pro Val Val Leu Asn Val Asp Ile Pro Asn Lys Arg Val  
                                  145                      150                      155                      160  
 30 Asp Val Glu Ile Leu Glu Gly Leu Asp Asp Glu Asp  
    165                      170  
 35 <210> 135  
     <211> 239  
     <212> PRT  
     <213> Streptococcus pneumoniae  
 40 <400> 135  
     Met Lys Ile Asp Ile Leu Thr Leu Phe Pro Glu Met Phe Ser Pro Leu  
         1                      5                      10                      15  
     Glu His Ser Ile Val Gly Lys Ala Arg Glu Lys Gly Leu Leu Asp Ile  
                                  20                      25                      30  
 45 Gln Tyr His Asn Phe Arg Glu Asn Ala Glu Lys Ala Arg His Val Asp  
                                  35                      40                      45  
 50 Asp Glu Pro Tyr Gly Gly Gly Gln Gly Met Leu Leu Arg Ala Gln Pro  
                                  50                      55                      60  
     Ile Phe Asp Ser Phe Asp Ala Ile Glu Lys Lys Asn Pro Arg Val Ile  
                                  65                      70                      75                      80  
 55 Leu Leu Asp Pro Ala Gly Lys Gln Phe Asp Gln Ala Tyr Ala Glu Asp  
    85                      90                      95

Leu Ala Gln Glu Glu Glu Leu Ile Phe Ile Cys Gly His Tyr Glu Gly  
                   100                  105                  110  
 5 Tyr Asp Glu Arg Ile Lys Thr Leu Val Thr Asp Glu Ile Ser Leu Gly  
                   115                  120                  125  
 Asp Tyr Val Leu Thr Gly Gly Glu Leu Ala Ala Met Thr Met Ile Asp  
                   130                  135                  140  
 10 Ala Thr Val Arg Leu Ile Pro Glu Val Ile Gly Lys Glu Ser Ser His  
                   145                  150                  155                  160  
 Gln Asp Asp Ser Phe Ser Ser Gly Leu Leu Glu Tyr His Gln Tyr Thr  
                   165                  170                  175  
 15 Arg Pro Tyr Asp Tyr Arg Gly Met Val Val Pro Asp Val Leu Met Ser  
                   180                  185                  190  
 20 Gly His His Glu Lys Ile Arg Gln Trp Arg Leu Tyr Glu Ser Leu Lys  
                   195                  200                  205  
 Lys Thr Tyr Glu Arg Arg Pro Asp Leu Leu Glu His Tyr Gln Leu Thr  
                   210                  215                  220  
 25 Val Glu Glu Glu Lys Met Leu Ala Glu Ile Lys Glu Asn Lys Glu  
                   225                  230                  235  
 30  
     <210> 136  
     <211> 186  
     <212> PRT  
 35 <213> Streptococcus pneumoniae  
     <400> 136  
 40 Met Ile Glu Ala Ser Lys Leu Lys Ala Gly Met Thr Phe Glu Thr Ala  
       1                  5                  10                  15  
 Asp Gly Lys Leu Ile Arg Val Leu Glu Ala Ser His His Lys Pro Gly  
                   20                  25                  30  
 45 Lys Gly Asn Thr Ile Met Arg Met Lys Leu Arg Asp Val Arg Thr Gly  
                   35                  40                  45  
 Ser Thr Phe Asp Thr Ser Tyr Arg Pro Glu Glu Lys Phe Glu Gln Ala  
                   50                  55                  60  
 50 Ile Ile Glu Thr Val Pro Ala Gln Tyr Leu Tyr Lys Met Asp Asp Thr  
                   65                  70                  75                  80  
 55 Ala Tyr Phe Met Asn Thr Glu Thr Tyr Asp Gln Tyr Glu Ile Pro Val  
                   85                  90                  95  
 Val Asn Val Glu Asn Glu Leu Leu Tyr Ile Leu Glu Asn Ser Asp Val

100                      105                      110  
 Lys Ile Gln Phe Tyr Gly Thr Glu Val Ile Gly Val Thr Val Pro Thr  
                     115                      120                      125  
 5 Thr Val Glu Leu Thr Val Ala Glu Thr Gln Pro Ser Ile Lys Gly Ala  
                     130                      135                      140  
 10 Thr Val Thr Gly Ser Gly Lys Pro Ala Thr Met Glu Thr Gly Leu Val  
                     145                      150                      155                      160  
 Val Asn Val Pro Asp Phe Ile Glu Ala Gly Gln Lys Leu Val Ile Asn  
                     165                      170                      175  
 15 Thr Ala Glu Gly Thr Tyr Val Ser Arg Ala  
                     180                      185  
 20 <210> 137  
     <211> 523  
     <212> PRT  
     <213> Streptococcus pneumoniae  
 25 <400> 137  
 Met Ala Phe Glu Ser Leu Thr Glu Arg Leu Gln Asn Val Phe Lys Asn  
     1                      5                      10                      15  
 30 Leu Arg Lys Lys Gly Lys Ile Ser Glu Ser Asp Val Gln Glu Ala Thr  
                     20                      25                      30  
 Lys Glu Ile Arg Leu Ala Leu Leu Glu Ala Asp Val Ala Leu Pro Val  
                     35                      40                      45  
 35 Val Lys Asp Phe Ile Lys Lys Val Arg Glu Arg Ala Val Gly His Glu  
                     50                      55                      60  
 Val Ile Asp Thr Leu Asn Pro Ala Gln Gln Ile Ile Lys Ile Val Asp  
     65                      70                      75                      80  
 40 Glu Glu Leu Thr Ala Val Leu Gly Ser Asp Thr Ala Glu Ile Ile Lys  
                     85                      90                      95  
 45 Ser Pro Lys Ile Pro Thr Ile Ile Met Met Val Gly Leu Gln Gly Ala  
                     100                      105                      110  
 Gly Lys Thr Thr Phe Ala Gly Lys Leu Ala Asn Lys Leu Lys Lys Glu  
                     115                      120                      125  
 50 Glu Asn Ala Arg Pro Leu Met Ile Ala Ala Asp Ile Tyr Arg Pro Ala  
                     130                      135                      140  
 Ala Ile Asp Gln Leu Lys Thr Leu Gly Gln Gln Ile Asp Val Pro Val  
     145                      150                      155                      160  
 55 Phe Ala Leu Gly Thr Glu Val Pro Ala Val Glu Ile Val Arg Gln Gly  
                     165                      170                      175

Leu Glu Gln Ala Gln Thr Asn His Asn Asp Tyr Val Leu Ile Asp Thr  
 180 185 190  
 5 Ala Gly Arg Leu Gln Ile Asp Glu Leu Leu Met Asn Glu Leu Arg Asp  
 195 200 205  
 Val Lys Thr Leu Ala Gln Pro Asn Glu Ile Leu Leu Val Val Asp Ala  
 210 215 220  
 10 Met Ile Gly Gln Glu Ala Ala Asn Val Ala Arg Glu Phe Asn Ala Gln  
 225 230 235 240  
 Leu Glu Val Thr Gly Val Ile Leu Thr Lys Ile Asp Gly Asp Thr Arg  
 245 250 255  
 15 Gly Gly Ala Ala Leu Ser Val Arg His Ile Thr Gly Lys Pro Ile Lys  
 260 265 270  
 20 Phe Thr Gly Thr Gly Glu Lys Ile Thr Asp Ile Glu Thr Phe His Pro  
 275 280 285  
 Asp Arg Met Ser Ser Arg Ile Leu Gly Met Gly Asp Met Leu Thr Leu  
 290 295 300  
 25 Ile Glu Lys Ala Ser Gln Glu Tyr Asp Glu Gln Lys Ala Leu Glu Met  
 305 310 315 320  
 Ala Glu Lys Met Arg Glu Asn Thr Phe Asp Phe Asn Asp Phe Ile Asp  
 325 330 335  
 30 Gln Leu Asp Gln Val Gln Asn Met Gly Pro Met Glu Asp Leu Leu Lys  
 340 345 350  
 35 Met Ile Pro Gly Met Ala Asn Asn Pro Ala Leu Gln Asn Met Lys Val  
 355 360 365  
 Asp Glu Arg Gln Ile Ala Arg Lys Arg Ala Ile Val Ser Ser Met Thr  
 370 375 380  
 40 Pro Glu Glu Arg Glu Asn Pro Asp Leu Leu Asn Pro Ser Arg Arg Arg  
 385 390 395 400  
 Arg Ile Ala Ala Gly Ser Gly Asn Thr Phe Val Glu Val Asn Lys Phe  
 405 410 415  
 45 Ile Lys Asp Phe Asn Gln Ala Lys Gln Leu Met Gln Gly Val Met Ser  
 420 425 430  
 50 Gly Asp Met Asn Lys Met Met Lys Gln Met Gly Ile Asn Pro Asn Asn  
 435 440 445  
 Leu Pro Lys Asn Met Pro Asn Met Gly Gly Met Asp Met Ser Ala Leu  
 450 455 460  
 55 Glu Gly Met Met Gly Gln Gly Gly Met Pro Asp Leu Ser Ala Leu Gly  
 465 470 475 480



Gly Ala Gly Met Pro Asp Met Ser Gln Met Phe Gly Gly Gly Leu Lys  
 485 490 495  
 5 Gly Lys Ile Gly Glu Phe Ala Met Lys Gln Ser Met Lys Arg Met Ala  
 500 505 510  
 Asn Lys Met Lys Lys Ala Lys Lys Lys Arg Lys  
 515 520  
 10  
 <210> 138  
 <211> 281  
 <212> PRT  
 15 <213> Streptococcus pneumoniae  
 <400> 138  
 Met Tyr Leu Ile Glu Ile Leu Lys Ser Ile Phe Phe Gly Ile Val Glu  
 1 5 10 15  
 20 Gly Ile Thr Glu Trp Leu Pro Ile Ser Ser Thr Gly His Leu Ile Leu  
 20 25 30  
 Ala Glu Glu Phe Ile Gln Tyr Gln Asn Gln Asn Glu Ala Phe Met Ser  
 25 35 40 45  
 Met Phe Asn Val Val Ile Gln Leu Gly Ala Ile Leu Ala Val Met Val  
 50 55 60  
 30 Ile Tyr Phe Asn Lys Leu Asn Pro Phe Lys Pro Thr Lys Asp Lys Gln  
 65 70 75 80  
 Glu Val Arg Lys Thr Trp Arg Leu Trp Leu Lys Val Leu Ile Ala Thr  
 85 90 95  
 35 Leu Pro Leu Leu Gly Val Phe Lys Phe Asp Asp Trp Phe Asp Thr His  
 100 105 110  
 Phe His Asn Met Val Ser Val Ala Leu Met Leu Ile Ile Tyr Gly Val  
 40 115 120 125  
 Ala Phe Ile Tyr Leu Glu Lys Arg Asn Lys Ala Arg Ala Ile Glu Pro  
 130 135 140  
 45 Ser Val Thr Glu Leu Asp Lys Leu Pro Tyr Thr Thr Ala Phe Tyr Ile  
 145 150 155 160  
 Gly Leu Phe Gln Val Leu Ala Leu Leu Pro Gly Thr Ser Arg Ser Gly  
 165 170 175  
 50 Ala Thr Ile Val Gly Gly Leu Leu Asn Gly Thr Ser Arg Ser Val Val  
 180 185 190  
 Thr Glu Phe Thr Phe Tyr Leu Gly Ile Pro Val Met Phe Gly Ala Ser  
 55 195 200 205  
 Ala Leu Lys Ile Phe Lys Phe Val Lys Ala Gly Glu Leu Leu Ser Phe

210                      215                      220  
 Gly Gln Leu Phe Leu Leu Leu Val Ala Met Gly Val Ala Phe Ala Val  
 225                      230                      235                      240  
 5 Ser Met Val Ala Ile Arg Phe Leu Thr Ser Tyr Val Lys Lys His Asp  
                     245                      250                      255  
 10 Phe Thr Leu Phe Gly Lys Tyr Arg Ile Val Leu Gly Ser Val Leu Leu  
                     260                      265                      270  
 Leu Tyr Ser Phe Val Arg Leu Phe Val  
                     275                      280  
 15  
 <210> 139  
 <211> 429  
 <212> PRT  
 <213> Streptococcus pneumoniae  
 20  
 <400> 139  
 Met Gly Leu Phe Asp Arg Leu Phe Gly Lys Lys Glu Glu Pro Lys Ile  
   1                      5                      10                      15  
 25 Glu Glu Val Val Lys Glu Ala Leu Glu Asn Leu Asp Leu Ser Glu Asp  
                     20                      25                      30  
 Ile Glu Pro Ala Phe Thr Glu Ala Glu Glu Val Ser Gln Glu Glu Ala  
                     35                      40                      45  
 30 Glu Val Glu Ser Ser Glu Glu Ser Val Phe Gln Glu Glu Asp Ser Gln  
                     50                      55                      60  
 35 Asp Thr Val Glu Glu Asn Leu Asp Leu Glu Pro Val Val Glu Val Ser  
                     65                      70                      75                      80  
 Gln Glu Glu Val Glu Glu Phe Pro Asn Ser Gln Glu Val Thr Glu Glu  
                     85                      90                      95  
 40 Glu Lys Leu Glu His Glu Gly Thr Val Glu Glu Asn Asn Phe Glu Val  
                     100                      105                      110  
 Leu Glu Pro Glu Ala Pro Gln Thr Glu Glu Thr Val Gln Glu Lys Tyr  
                     115                      120                      125  
 45 Asp Arg Ser Leu Lys Lys Thr Arg Thr Gly Phe Gly Ala Arg Leu Asn  
                     130                      135                      140  
 50 Ala Phe Phe Ala Asn Phe Arg Ser Val Asp Glu Glu Phe Phe Glu Glu  
                     145                      150                      155                      160  
 Leu Glu Glu Leu Leu Ile Met Ser Asp Val Gly Val Gln Val Ala Ser  
                     165                      170                      175  
 55 Asn Leu Thr Glu Glu Leu Arg Tyr Glu Ala Lys Leu Glu Asn Ala Lys  
                     180                      185                      190

Lys Pro Asp Ala Leu Arg Arg Val Ile Ile Glu Lys Leu Val Glu Leu  
 195 200 205  
 5 Tyr Glu Lys Asp Gly Ser Tyr Asp Glu Ser Ile His Phe Gln Asp Asn  
 210 215 220  
 Leu Thr Val Met Leu Phe Val Gly Val Asn Gly Val Gly Lys Thr Thr  
 225 230 235 240  
 10 Ser Ile Gly Lys Leu Ala His Arg Tyr Lys Arg Ala Gly Lys Lys Val  
 245 250 255  
 Met Leu Val Ala Ala Asp Thr Phe Arg Ala Gly Ala Val Ala Gln Leu  
 260 265 270  
 15 Ala Glu Trp Gly Arg Arg Val Asp Val Pro Val Val Thr Gly Pro Glu  
 275 280 285  
 Lys Ala Asp Pro Ala Ser Val Val Phe Asp Gly Met Glu Arg Ala Val  
 290 295 300  
 Ala Glu Gly Ile Asp Ile Leu Met Ile Asp Thr Ala Gly Arg Leu Gln  
 305 310 315 320  
 25 Asn Lys Asp Asn Leu Met Ala Glu Leu Glu Lys Ile Gly Arg Ile Ile  
 325 330 335  
 Lys Arg Val Val Pro Glu Ala Pro His Glu Thr Phe Leu Ala Leu Asp  
 340 345 350  
 30 Ala Ser Thr Gly Gln Asn Ala Leu Val Gln Ala Lys Glu Phe Ser Lys  
 355 360 365  
 Ile Thr Pro Leu Thr Gly Ile Val Leu Thr Lys Ile Asp Gly Thr Ala  
 370 375 380  
 Arg Gly Gly Val Val Leu Ala Ile Arg Glu Glu Leu Asn Ile Pro Val  
 385 390 395 400  
 40 Lys Leu Ile Gly Phe Gly Glu Lys Ile Asp Asp Ile Gly Glu Phe Asn  
 405 410 415  
 Ser Glu Asn Phe Met Lys Gly Leu Leu Glu Gly Leu Ile  
 420 425  
 45  
 <210> 140  
 <211> 165  
 <212> PRT  
 50 <213> Streptococcus pneumoniae  
 <400> 140  
 Met Tyr Ile Glu Met Val Asp Glu Thr Gly Gln Val Ser Lys Glu Met  
 1 5 10 15  
 55 Leu Gln Gln Thr Gln Glu Ile Leu Glu Phe Ala Ala Lys Lys Leu Gly  
 20 25 30

Lys Glu Asp Lys Glu Met Ala Val Thr Phe Val Thr Asn Glu Arg Ser  
 35 40 45  
 5 His Glu Leu Asn Leu Glu Tyr Arg Asp Thr Asp Arg Pro Thr Asp Val  
 50 55 60  
 Ile Ser Leu Glu Tyr Lys Pro Glu Leu Glu Ile Ala Phe Asp Glu Glu  
 65 70 75 80  
 10 Asp Leu Leu Glu Asn Pro Glu Leu Ala Glu Met Met Ser Glu Phe Asp  
 85 90 95  
 Ala Tyr Ile Gly Glu Leu Phe Ile Ser Ile Asp Lys Ala His Glu Gln  
 100 105 110  
 15 Ala Glu Glu Tyr Gly His Ser Phe Glu Arg Glu Met Gly Phe Leu Ala  
 115 120 125  
 20 Val His Gly Phe Leu His Ile Asn Gly Tyr Asp His Tyr Thr Pro Glu  
 130 135 140  
 Glu Glu Ala Glu Met Phe Gly Leu Gln Glu Glu Ile Leu Thr Ala Tyr  
 145 150 155 160  
 25 Gly Leu Thr Arg Gln  
 165  
 30 <210> 141  
 <211> 255  
 <212> PRT  
 <213> Streptococcus pneumoniae  
 35 <400> 141  
 Met Ser Ile Arg Val Ile Ile Ala Gly Phe Lys Gly Lys Met Gly Gln  
 1 5 10 15  
 40 Ala Ala Cys Gln Met Val Leu Thr Asp Pro Asp Leu Asp Leu Val Ala  
 20 25 30  
 Val Leu Asp Pro Phe Glu Ser Glu Ser Glu Trp Gln Gly Ile Pro Val  
 35 40 45  
 45 Phe Lys Asp Lys Ala Asp Leu Ala Gly Phe Glu Ala Asp Val Trp Val  
 50 55 60  
 Asp Phe Thr Thr Pro Ala Val Ala Tyr Glu Asn Thr Arg Phe Ala Leu  
 65 70 75 80  
 50 Glu Asn Gly Phe Ala Pro Val Val Gly Thr Thr Gly Phe Thr Ser Glu  
 85 90 95  
 55 Glu Ile Ala Glu Leu Lys Glu Phe Ser Arg Ala Gln Asp Leu Gly Gly  
 100 105 110  
 Leu Ile Ala Pro Asn Phe Ala Leu Gly Ala Val Leu Leu Met Gln Phe

115                      120                      125  
 Ala Thr Gln Ala Ala Lys Tyr Phe Pro Asn Val Glu Ile Ile Glu Leu  
 130                      135                      140  
 5 His His Asp Lys Lys Lys Asp Ala Pro Ser Gly Thr Ala Ile Lys Thr  
 145                      150                      155                      160  
 10 Ala Glu Leu Met Ala Glu Val Arg Glu Ser Ile Gln Gln Gly Ala Ala  
 165                      170                      175  
 Asp Glu Glu Glu Leu Ile Ala Gly Ala Arg Gly Ala Asp Phe Asp Gly  
 180                      185                      190  
 15 Met Arg Ile His Ser Val Arg Leu Pro Gly Leu Val Ala His Gln Glu  
 195                      200                      205  
 Val Ile Phe Gly Asn Gln Gly Glu Gly Leu Thr Leu Arg His Asp Ser  
 210                      215                      220  
 20 Tyr Asp Arg Ile Ser Phe Met Thr Gly Val Asn Leu Gly Ile Lys Glu  
 225                      230                      235                      240  
 Val Val Lys Arg His Glu Leu Val Tyr Gly Leu Glu His Leu Leu  
 245                      250                      255  
 25  
 <210> 142  
 <211> 91  
 30 <212> PRT  
 <213> Streptococcus pneumoniae  
 <400> 142  
 Met Ala Asn Lys Gln Asp Leu Ile Ala Lys Val Ala Glu Ala Thr Glu  
 1                      5                      10                      15  
 Leu Thr Lys Lys Asp Ser Ala Ala Ala Val Glu Ala Val Phe Ala Ala  
 20                      25                      30  
 40 Val Ala Asp Tyr Leu Ala Ala Gly Glu Lys Val Gln Leu Ile Gly Phe  
 35                      40                      45  
 Ser Asn Phe Glu Val Arg Glu Arg Ala Glu Arg Lys Gly Arg Asn Pro  
 50                      55                      60  
 45 Gln Thr Gly Lys Glu Met Thr Ile Ala Ala Ser Lys Val Pro Ala Phe  
 65                      70                      75                      80  
 Lys Ala Gly Lys Ala Leu Lys Asp Ala Val Lys  
 85                      90  
 50  
 <210> 143  
 <211> 306  
 55 <212> PRT  
 <213> Streptococcus pneumoniae

<400> 143  
 Met Thr Lys Thr Ala Phe Leu Phe Ala Gly Gln Gly Ala Gln Tyr Leu  
 1 5 10 15  
 5 Gly Met Gly Arg Asp Phe Tyr Asp Gln Tyr Pro Ile Val Lys Glu Thr  
 20 25 30  
 Ile Asp Arg Ala Ser Gln Val Leu Gly Tyr Asp Leu Arg Tyr Leu Ile  
 35 40 45  
 10 Asp Thr Glu Glu Asp Lys Leu Asn Gln Thr Arg Tyr Thr Gln Pro Ala  
 50 55 60  
 15 Ile Leu Ala Thr Ser Val Ala Ile Tyr Arg Leu Leu Gln Glu Lys Gly  
 65 70 75 80  
 Tyr Gln Pro Asp Met Val Ala Gly Leu Ser Leu Gly Glu Tyr Ser Ala  
 85 90 95  
 20 Leu Val Ala Ser Gly Ala Leu Asp Phe Glu Asp Ala Val Ala Leu Val  
 100 105 110  
 Ala Lys Arg Gly Ala Tyr Met Glu Glu Ala Ala Pro Ala Asp Ser Gly  
 115 120 125  
 25 Lys Met Val Ala Val Leu Asn Thr Pro Val Glu Val Ile Glu Glu Ala  
 130 135 140  
 30 Cys Gln Lys Ala Ser Glu Leu Gly Val Val Thr Pro Ala Asn Tyr Asn  
 145 150 155 160  
 Thr Pro Ala Gln Ile Val Ile Ala Gly Glu Val Val Ala Val Asp Arg  
 165 170 175  
 35 Ala Val Glu Leu Leu Gln Glu Ala Gly Ala Lys Arg Leu Ile Pro Leu  
 180 185 190  
 Lys Val Ser Gly Pro Phe His Thr Ala Leu Leu Glu Pro Ala Ser Gln  
 195 200 205  
 40 Lys Leu Ala Glu Thr Leu Ala Gln Val Ser Phe Ser Asp Phe Thr Cys  
 210 215 220  
 45 Pro Leu Val Gly Asn Thr Glu Ala Ala Val Met Gln Lys Glu Asp Ile  
 225 230 235 240  
 Ala Gln Leu Leu Thr Arg Gln Val Lys Glu Pro Val Arg Phe Tyr Glu  
 245 250 255  
 50 Ser Ile Gly Val Met Gln Glu Ala Gly Ile Ser Asn Phe Ile Glu Ile  
 260 265 270  
 Gly Pro Gly Lys Val Leu Ser Gly Phe Val Lys Lys Ile Asp Gln Thr  
 275 280 285  
 55 Ala His Leu Ala His Val Glu Asp Gln Ala Ser Leu Val Ala Leu Leu  
 290 295 300

Glu Lys  
305

5  
<210> 144  
<211> 243  
<212> PRT  
<213> Streptococcus pneumoniae

10  
<400> 144  
Met Lys Leu Glu His Lys Asn Ile Phe Ile Thr Gly Ser Ser Arg Gly  
1 5 10 15

15  
Ile Gly Leu Ala Ile Ala His Lys Phe Ala Gln Ala Gly Ala Asn Ile  
20 25 30

Val Leu Asn Ser Arg Gly Ala Ile Ser Glu Glu Leu Leu Ala Glu Phe  
35 40 45

20  
Ser Asn Tyr Gly Ile Lys Val Val Pro Ile Ser Gly Asp Val Ser Asp  
50 55 60

Phe Ala Asp Ala Lys Arg Met Ile Asp Gln Ala Ile Ala Glu Leu Gly  
25 65 70 75 80

Ser Val Asp Val Leu Val Asn Asn Ala Gly Ile Thr Gln Asp Thr Leu  
85 90 95

30  
Met Leu Lys Met Thr Glu Ala Asp Phe Glu Lys Val Leu Lys Val Asn  
100 105 110

Leu Thr Gly Ala Phe Asn Met Thr Gln Ser Val Leu Lys Pro Met Met  
115 120 125

35  
Lys Ala Arg Glu Gly Ala Ile Ile Asn Met Ser Ser Val Val Gly Leu  
130 135 140

40  
Met Gly Asn Ile Gly Gln Ala Asn Tyr Ala Ala Ser Lys Ala Gly Leu  
145 150 155 160

Ile Gly Phe Thr Lys Ser Val Ala Arg Glu Val Ala Ser Arg Asn Ile  
165 170 175

45  
Arg Val Asn Val Ile Ala Pro Gly Met Ile Glu Ser Asp Met Thr Ala  
180 185 190

Ile Leu Ser Asp Lys Ile Lys Glu Ala Thr Leu Ala Gln Ile Pro Met  
195 200 205

50  
Lys Glu Phe Gly Gln Ala Glu Gln Val Ala Asp Leu Thr Val Phe Leu  
210 215 220

55  
Ala Gly Gln Asp Tyr Leu Thr Gly Gln Val Val Ala Ile Asp Gly Gly  
225 230 235 240

Leu Ser Met

5 <210> 145  
 <211> 276  
 <212> PRT  
 <213> Streptococcus pneumoniae  
  
 <400> 145  
 10 Met Gly Val Lys Lys Lys Leu Lys Leu Thr Ser Leu Leu Gly Leu Ser  
     1                    5                    10                    15  
     Leu Leu Ile Met Thr Ala Cys Ala Thr Asn Gly Val Thr Ser Asp Ile  
                     20                    25                    30  
 15 Thr Ala Glu Ser Ala Asp Phe Trp Ser Lys Leu Val Tyr Phe Phe Ala  
                     35                    40                    45  
     Glu Ile Ile Arg Phe Leu Ser Phe Asp Ile Ser Ile Gly Val Gly Ile  
 20                    50                    55                    60  
     Ile Leu Phe Thr Val Leu Ile Arg Thr Val Leu Leu Pro Val Phe Gln  
     65                    70                    75                    80  
 25 Val Gln Met Val Ala Ser Arg Lys Met Gln Glu Ala Gln Pro Arg Ile  
                     85                    90                    95  
     Lys Ala Leu Arg Glu Gln Tyr Pro Gly Arg Asp Met Glu Ser Arg Thr  
                     100                    105                    110  
 30 Lys Leu Glu Gln Glu Met Arg Lys Val Phe Lys Glu Met Gly Val Arg  
                     115                    120                    125  
     Gln Ser Asp Ser Leu Trp Pro Ile Leu Ile Gln Met Pro Val Ile Leu  
 35                    130                    135                    140  
     Ala Leu Phe Gln Ala Leu Ser Arg Val Asp Phe Leu Lys Thr Gly His  
     145                    150                    155                    160  
 40 Phe Leu Trp Ile Asn Leu Gly Ser Val Asp Thr Thr Leu Val Leu Pro  
                     165                    170                    175  
     Ile Leu Ala Ala Val Phe Thr Phe Leu Ser Thr Trp Leu Ser Asn Lys  
                     180                    185                    190  
 45 Ala Leu Ser Glu Arg Asn Gly Ala Thr Thr Ala Met Met Tyr Gly Ile  
                     195                    200                    205  
     Pro Val Leu Ile Phe Ile Phe Ala Val Tyr Ala Pro Gly Gly Val Ala  
 50                    210                    215                    220  
     Leu Tyr Trp Thr Val Ser Asn Ala Tyr Gln Val Leu Gln Thr Tyr Phe  
     225                    230                    235                    240  
 55 Leu Asn Asn Pro Phe Lys Ile Ile Ala Glu Arg Glu Ala Val Val Gln  
                     245                    250                    255



Ala Gln Lys Asp Leu Glu Asn Arg Lys Arg Lys Ala Lys Lys Lys Ala  
 260 265 270

5 Gln Lys Thr Lys  
 275

10 <210> 146  
 <211> 409  
 <212> PRT  
 <213> Streptococcus pneumoniae

15 <400> 146  
 Met Lys Ile Ser Lys Arg His Leu Leu Asn Tyr Ser Ile Leu Ile Pro  
 1 5 10 15

Tyr Leu Leu Leu Ser Ile Leu Gly Leu Ile Val Val Tyr Ser Thr Thr  
 20 25 30

20 Ser Ala Ile Leu Ile Glu Glu Gly Lys Ser Ala Leu Gln Leu Val Arg  
 35 40 45

25 Asn Gln Gly Ile Phe Trp Ile Val Ser Leu Ile Leu Ile Ala Leu Ile  
 50 55 60

Tyr Lys Leu Arg Leu Asp Phe Leu Arg Asn Glu Arg Leu Ile Ile Leu  
 65 70 75 80

30 Val Ile Leu Ile Glu Met Leu Leu Leu Phe Leu Ala Arg Phe Ile Gly  
 85 90 95

Ile Ser Val Asn Gly Ala Tyr Gly Trp Ile Ser Val Ala Gly Val Thr  
 100 105 110

35 Ile Gln Pro Ala Glu Tyr Leu Lys Ile Ile Ile Ile Trp Tyr Leu Ala  
 115 120 125

40 His Arg Phe Ser Lys Gln Gln Glu Glu Ile Ala Thr Tyr Asp Phe Gln  
 130 135 140

Val Leu Thr Gln Asn Gln Trp Leu Pro Arg Ala Phe Asn Asp Trp Arg  
 145 150 155 160

45 Phe Val Leu Leu Val Leu Ile Gly Ser Leu Gly Ile Phe Pro Asp Leu  
 165 170 175

Gly Asn Ala Thr Ile Leu Val Leu Val Ser Leu Ile Met Tyr Thr Val  
 180 185 190

50 Ser Gly Ile Ala Tyr Arg Trp Phe Ser Thr Ile Leu Ala Leu Val Ser  
 195 200 205

55 Ala Thr Ser Val Phe Val Leu Thr Thr Ile Ser Leu Ile Gly Val Glu  
 210 215 220

Thr Phe Ser Lys Ile Pro Val Phe Gly Tyr Val Ala Lys Arg Phe Ser  
 225 230 235 240

86

	85	90	95
	Ile Asn Leu Ser Gly Lys Lys Leu Asp Gln Thr Ala Leu Pro Met Gln		
	100	105	110
5	Val Thr Gln Phe Asp Phe Glu Asp Lys Leu Phe Ile Lys Gly Leu Val		
	115	120	125
	Leu Glu Glu Glu Lys Thr Phe Ala Val Asp His Asp Ala Thr Val Val		
10	130	135	140
	Glu Ala Asp Gly Thr Glu Val Arg Ile Ala Pro Leu Asp Val Gln Tyr		
	145	150	155
	Gln Asn Ala Thr Ile Trp Gly Lys Leu Ile Thr Asn Phe Ala Gly Pro		
15	165	170	175
	Met Asn Asn Phe Ile Leu Gly Val Val Val Phe Trp Val Leu Ile Phe		
	180	185	190
20	Met Gln Gly Gly Val Arg Asp Val Asp Thr Asn Gln Phe His Ile Met		
	195	200	205
	Pro Gln Gly Ala Leu Ala Lys Val Gly Val Pro Glu Thr Ala Gln Ile		
25	210	215	220
	Thr Lys Ile Gly Ser His Glu Val Ser Asn Trp Glu Ser Leu Ile Gln		
	225	230	235
	Ala Val Glu Thr Glu Thr Lys Asp Lys Thr Ala Pro Thr Leu Asp Val		
30	245	250	255
	Thr Ile Ser Glu Lys Gly Ser Asp Lys Gln Val Thr Val Thr Pro Glu		
	260	265	270
35	Asp Ser Gln Gly Arg Tyr Leu Leu Gly Val Gln Pro Gly Val Lys Ser		
	275	280	285
	Asp Phe Leu Ser Met Phe Val Gly Gly Phe Thr Thr Ala Ala Asp Ser		
40	290	295	300
	Ala Leu Arg Ile Leu Ser Ala Leu Lys Asn Leu Ile Phe Gln Pro Asp		
	305	310	315
	Leu Asn Lys Leu Gly Gly Pro Val Ala Ile Phe Lys Ala Ser Ser Asp		
45	325	330	335
	Ala Ala Lys Asn Gly Ile Glu Asn Ile Leu Tyr Phe Leu Ala Met Ile		
	340	345	350
50	Ser Ile Asn Ile Gly Ile Phe Asn Leu Ile Pro Ile Pro Ala Leu Asp		
	355	360	365
	Gly Gly Lys Ile Val Leu Asn Ile Leu Glu Ala Ile Arg Arg Lys Pro		
55	370	375	380
	Leu Lys Gln Glu Ile Glu Thr Tyr Val Thr Leu Ala Gly Val Val Ile		

385                      390                      395                      400

Met Val Val Leu Met Ile Ala Val Thr Trp Asn Asp Ile Met Arg Leu  
                                  405                      410                      415

5      Phe Phe Arg

10     <210> 148  
        <211> 197  
        <212> PRT  
        <213> Streptococcus pneumoniae

15     <400> 148  
        Met Tyr Ala Tyr Leu Lys Gly Ile Ile Thr Lys Ile Thr Ala Lys Tyr  
              1                      5                      10                      15

20     Ile Val Leu Glu Thr Asn Gly Ile Gly Tyr Ile Leu His Val Ala Asn  
                                  20                      25                      30

       Pro Tyr Ala Tyr Ser Gly Gln Val Asn Gln Glu Ala Gln Ile Tyr Val  
                                  35                      40                      45

25     His Gln Val Val Arg Glu Asp Ala His Leu Leu Tyr Gly Phe Arg Ser  
              50                      55                      60

       Glu Asp Glu Lys Lys Leu Phe Leu Ser Leu Ile Ser Val Ser Gly Ile  
              65                      70                      75                      80

30     Gly Pro Val Ser Ala Leu Ala Ile Ile Ala Ala Asp Asp Asn Ala Gly  
                                  85                      90                      95

       Leu Val Gln Ala Ile Glu Thr Lys Asn Ile Thr Tyr Leu Thr Lys Phe  
              100                      105                      110

       Pro Lys Ile Gly Lys Lys Thr Ala Gln Gln Met Val Leu Asp Leu Glu  
              115                      120                      125

40     Gly Lys Val Val Val Ala Gly Asp Asp Leu Pro Ala Lys Val Ala Val  
              130                      135                      140

       Gln Ala Ser Ala Glu Asn Gln Glu Leu Glu Glu Ala Met Glu Ala Met  
              145                      150                      155                      160

45     Leu Ala Leu Gly Tyr Lys Ala Thr Glu Leu Lys Lys Ile Lys Lys Phe  
                                  165                      170                      175

       Phe Glu Gly Thr Thr Asp Thr Ala Glu Asn Tyr Ile Lys Ser Ala Leu  
              180                      185                      190

50     Lys Met Leu Val Lys  
              195

55     <210> 149  
        <211> 257

&lt;212&gt; PRT

&lt;213&gt; Streptococcus pneumoniae

&lt;400&gt; 149

5 Met Lys Asn Asn Arg Ile Leu Ala Leu Ser Gly Asn Asp Ile Phe Ser  
    1                      5                      10                      15  
    Gly Gly Gly Leu Ser Ala Asp Leu Ala Thr Tyr Thr Leu Asn Gly Leu  
                   20                      25                      30  
 10 His Gly Phe Val Ala Val Thr Cys Leu Thr Ala Leu Thr Glu Lys Gly  
                   35                      40                      45  
    Phe Glu Val Phe Pro Thr Asp Asp Thr Ile Phe Gln His Glu Leu Asp  
 15                  50                      55                      60  
    Ser Leu Arg Asp Val Glu Phe Gly Gly Ile Lys Ile Gly Leu Leu Pro  
                   65                      70                      75                      80  
 20 Thr Val Ser Val Ala Glu Lys Ala Leu Asp Phe Ile Lys Gln Arg Pro  
                   85                      90                      95  
    Gly Val Pro Val Val Leu Asp Pro Val Leu Val Cys Lys Glu Thr His  
                   100                      105                      110  
 25 Asp Val Ala Val Ser Glu Leu Cys Gln Glu Leu Ile Arg Phe Phe Pro  
                   115                      120                      125  
    Tyr Val Ser Val Ile Thr Pro Asn Leu Pro Glu Ala Glu Leu Leu Ser  
 30                  130                      135                      140  
    Gly Gln Glu Ile Lys Thr Leu Glu Asp Met Lys Thr Ala Ala Gln Lys  
                   145                      150                      155                      160  
 35 Leu His Asp Leu Gly Ala Pro Ala Val Ile Ile Lys Gly Gly Asn Arg  
                   165                      170                      175  
    Leu Ser Gln Asp Lys Ala Val Asp Val Phe Tyr Asp Gly Gln Thr Phe  
                   180                      185                      190  
 40 Thr Ile Leu Glu Asn Pro Val Ile Gln Gly Gln Asn Ala Gly Ala Gly  
                   195                      200                      205  
    Cys Thr Phe Ala Ser Ser Ile Ala Ser His Leu Val Lys Gly Asp Lys  
 45                  210                      215                      220  
    Phe Leu Pro Ala Val Glu Ser Ser Lys Ala Phe Val Tyr Arg Ala Ile  
                   225                      230                      235                      240  
 50 Ala Gln Ala Asp Gln Tyr Gly Val Arg Gln Tyr Glu Ala Asn Lys Asn  
                   245                      250                      255

Asn

55

&lt;210&gt; 150

&lt;211&gt; 412

&lt;212&gt; PRT

&lt;213&gt; Streptococcus pneumoniae

5 <400> 150  
 Met Ile Glu Thr Glu Lys Lys Glu Glu Arg Val Leu Leu Ile Gly Val  
 1 5 10 15

10 Glu Leu Gln Gly Met Asp Ser Phe Asp Leu Ser Met Glu Glu Leu Ala  
 20 25 30

Ser Leu Ala Lys Thr Ala Gly Ala Val Val Val Asp Ser Tyr Arg Gln  
 35 40 45

15 Lys Arg Glu Lys Tyr Asp Ser Lys Thr Phe Val Gly Ser Gly Lys Leu  
 50 55 60

Glu Glu Ile Ala Leu Met Val Asp Ala Glu Glu Ile Thr Thr Val Ile  
 65 70 75 80

20 Val Asn Asn Arg Leu Thr Pro Arg Gln Asn Val Asn Leu Glu Glu Val  
 85 90 95

25 Leu Gly Val Lys Val Ile Asp Arg Met Gln Leu Ile Leu Asp Ile Phe  
 100 105 110

Ala Met Arg Ala Arg Ser His Glu Gly Lys Leu Gln Val His Leu Ala  
 115 120 125

30 Gln Phe Lys Tyr Leu Leu Pro Arg Leu Val Gly Gln Gly Ile Met Leu  
 130 135 140

Ser Arg Gln Ala Gly Gly Ile Gly Ser Arg Gly Pro Gly Glu Ser Gln  
 145 150 155 160

35 Leu Glu Leu Asn Arg Arg Ser Val Arg Asn Gln Ile Thr Asp Ile Glu  
 165 170 175

40 Arg Gln Leu Lys Val Val Glu Lys Asn Arg Ala Thr Val Arg Glu Lys  
 180 185 190

Arg Leu Glu Ser Ser Thr Phe Lys Ile Gly Leu Ile Gly Tyr Thr Asn  
 195 200 205

45 Ala Gly Lys Ser Thr Ile Met Asn Ile Leu Thr Ser Lys Thr Gln Tyr  
 210 215 220

Glu Ala Asp Glu Leu Phe Ala Thr Leu Asp Ala Thr Thr Lys Ser Ile  
 225 230 235 240

50 His Leu Gly Gly Asn Leu Gln Val Thr Leu Thr Asp Thr Val Gly Phe  
 245 250 255

55 Ile Gln Asp Leu Pro Thr Glu Leu Val Ser Ser Phe Lys Ser Thr Leu  
 260 265 270

Glu Glu Ser Lys His Val Asp Leu Leu Val His Val Ile Asp Ala Ser

275                      280                      285  
 Asn Pro Tyr His Glu Glu His Glu Lys Thr Val Leu Ser Ile Met Lys  
 290                      295                      300  
 5 Asp Leu Asp Met Glu Asp Ile Pro His Leu Thr Leu Tyr Asn Lys Ala  
 305                      310                      315                      320  
 10 Asp Leu Val Glu Asp Phe Thr Pro Thr Gln Thr Pro Tyr Thr Leu Ile  
 325                      330                      335  
 Ser Ala Lys Ser Glu Asp Ser Arg Glu Asn Leu Gln Ala Leu Leu Leu  
 340                      345                      350  
 15 Asp Lys Ile Lys Glu Ile Phe Glu Ala Phe Thr Leu Arg Val Pro Phe  
 355                      360                      365  
 Ser Lys Ser Tyr Lys Ile His Asp Leu Glu Ser Val Ala Ile Leu Glu  
 370                      375                      380  
 20 Glu Arg Asp Tyr Gln Glu Asp Gly Glu Val Ile Thr Gly Tyr Ile Ser  
 385                      390                      395                      400  
 25 Glu Lys Asn Lys Trp Arg Leu Glu Glu Phe Tyr Asp  
 405                      410  
 <210> 151  
 <211> 160  
 30 <212> PRT  
 <213> Streptococcus pneumoniae  
 <400> 151  
 35 Met Ala Glu Lys Thr Tyr Pro Met Thr Leu Glu Glu Lys Glu Lys Leu  
 1                      5                      10                      15  
 Glu Lys Glu Leu Glu Glu Leu Lys Leu Val Arg Arg Pro Glu Val Val  
 20                      25                      30  
 40 Glu Arg Ile Lys Ile Ala Arg Ser Tyr Gly Asp Leu Ser Glu Asn Ser  
 35                      40                      45  
 Glu Tyr Glu Ala Ala Lys Asp Glu Gln Ala Phe Val Glu Gly Gln Ile  
 50                      55                      60  
 45 Ser Ser Leu Glu Thr Lys Ile Arg Tyr Ala Glu Ile Val Asn Ser Asp  
 65                      70                      75                      80  
 50 Ala Val Ala Gln Asp Glu Val Ala Ile Gly Lys Thr Val Thr Ile Gln  
 85                      90                      95  
 Glu Ile Gly Glu Asp Glu Glu Glu Val Tyr Ile Ile Val Gly Ser Ala  
 100                      105                      110  
 55 Gly Ala Asp Ala Phe Ala Gly Lys Val Ser Asn Glu Ser Pro Ile Gly  
 115                      120                      125

Gln Ala Leu Ile Gly Lys Lys Thr Gly Asp Thr Ala Thr Ile Glu Thr  
 130 135 140

5 Pro Val Gly Ser Tyr Asp Val Lys Ile Leu Lys Val Glu Lys Thr Ala  
 145 150 155 160

10  
 <210> 152  
 <211> 189  
 <212> PRT  
 <213> Streptococcus pneumoniae

15  
 <400> 152  
 Met Thr Lys Leu Leu Val Gly Leu Gly Asn Pro Gly Asp Lys Tyr Phe  
 1 5 10 15

20 Glu Thr Lys His Asn Val Gly Phe Met Leu Ile Asp Gln Leu Ala Lys  
 20 25 30

Lys Gln Asn Val Thr Phe Thr His Asp Lys Ile Phe Gln Ala Asp Leu  
 35 40 45

25 Ala Ser Phe Phe Leu Asn Gly Glu Lys Ile Tyr Leu Val Lys Pro Thr  
 50 55 60

30 Thr Phe Met Asn Glu Ser Gly Lys Ala Val His Ala Leu Leu Thr Tyr  
 65 70 75 80

Tyr Gly Leu Asp Ile Asp Asp Leu Leu Ile Ile Tyr Asp Asp Leu Asp  
 85 90 95

35 Met Glu Val Gly Lys Ile Arg Leu Arg Ala Lys Gly Ser Ala Gly Gly  
 100 105 110

His Asn Gly Ile Lys Ser Ile Ile Gln His Ile Gly Thr Gln Val Phe  
 115 120 125

40 Asn Arg Val Lys Ile Gly Ile Gly Arg Pro Lys Asn Gly Met Ser Val  
 130 135 140

45 Val His His Val Leu Ser Lys Phe Asp Arg Asp Glu Tyr Ile Gly Ile  
 145 150 155 160

Leu Gln Ser Val Asp Lys Val Asp Asp Ser Val Asn Tyr Tyr Leu Gln  
 165 170 175

50 Glu Lys Asn Phe Glu Lys Thr Met Gln Arg Tyr Asn Gly  
 180 185

55  
 <210> 153  
 <211> 283  
 <212> PRT  
 <213> Streptococcus pneumoniae



<400> 153  
 Met Ile Leu Ile Thr Gly Ala Asn Gly Gln Leu Gly Thr Glu Leu Arg  
 1 5 10 15  
 5 Tyr Leu Leu Asp Glu Arg Asn Glu Glu Tyr Val Ala Val Asp Val Ala  
 20 25 30  
 10 Lys Met Asp Ile Thr Asn Glu Glu Met Val Glu Lys Val Phe Glu Glu  
 35 40 45  
 Val Lys Pro Thr Leu Val Tyr His Cys Ala Ala Tyr Thr Ala Val Asp  
 50 55 60  
 15 Ala Ala Glu Asp Glu Gly Lys Glu Leu Asp Phe Ala Ile Asn Val Thr  
 65 70 75 80  
 Gly Thr Lys Asn Val Ala Lys Ala Ser Glu Lys His Gly Ala Thr Leu  
 85 90 95  
 20 Val Tyr Ile Ser Thr Asp Tyr Val Phe Asp Gly Lys Lys Pro Val Gly  
 100 105 110  
 25 Gln Glu Trp Glu Val Asp Asp Arg Pro Asp Pro Gln Thr Glu Tyr Gly  
 115 120 125  
 Arg Thr Lys Arg Met Gly Glu Leu Val Glu Lys His Val Ser Asn  
 130 135 140  
 30 Phe Tyr Ile Ile Arg Thr Ala Trp Val Phe Gly Asn Tyr Gly Lys Asn  
 145 150 155 160  
 Phe Val Phe Thr Met Gln Asn Leu Ala Lys Thr His Lys Thr Leu Thr  
 165 170 175  
 35 Val Val Asn Asp Gln Tyr Gly Arg Pro Thr Trp Thr Arg Thr Leu Ala  
 180 185 190  
 40 Glu Phe Met Thr Tyr Leu Ala Glu Asn Arg Lys Glu Phe Gly Tyr Tyr  
 195 200 205  
 His Leu Ser Asn Asp Ala Thr Glu Asp Thr Thr Trp Tyr Asp Phe Ala  
 210 215 220  
 45 Val Glu Ile Leu Lys Asp Thr Asp Val Glu Val Lys Pro Val Asp Ser  
 225 230 235 240  
 Ser Gln Phe Pro Ala Lys Ala Lys Arg Pro Leu Asn Ser Thr Met Ser  
 245 250 255  
 50 Leu Ala Lys Ala Lys Ala Thr Gly Phe Val Ile Pro Thr Trp Gln Asp  
 260 265 270  
 55 Ala Leu Gln Glu Phe Tyr Lys Gln Glu Val Arg  
 275 280

<210> 154  
 <211> 407  
 5 <212> PRT  
 <213> Streptococcus pneumoniae  
  
 <400> 154  
 10 Met Lys Arg Ser Leu Asp Ser Arg Val Asp Tyr Ser Leu Leu Leu Pro  
     1                    5                    10                    15  
 Val Phe Phe Leu Leu Val Ile Gly Val Val Ala Ile Tyr Ile Ala Val  
                     20                    25                    30  
 15 Ser His Asp Tyr Pro Asn Asn Ile Leu Pro Ile Leu Gly Gln Gln Val  
                     35                    40                    45  
 Ala Trp Ile Ala Leu Gly Leu Val Ile Gly Phe Val Val Met Leu Phe  
                     50                    55                    60  
 20 Asn Thr Glu Phe Leu Trp Lys Val Thr Pro Phe Leu Tyr Ile Leu Gly  
                     65                    70                    75                    80  
 Leu Gly Leu Met Ile Leu Pro Ile Val Phe Tyr Asn Pro Ser Leu Val  
 25                    85                    90                    95  
 Ala Ser Thr Gly Ala Lys Asn Trp Val Ser Ile Asn Gly Ile Thr Leu  
                     100                    105                    110  
 30 Phe Gln Pro Ser Glu Phe Met Lys Ile Ser Tyr Ile Leu Met Leu Ala  
                     115                    120                    125  
 Arg Val Ile Val Gln Phe Thr Lys Lys His Lys Glu Trp Arg Arg Thr  
                     130                    135                    140  
 35 Val Pro Leu Asp Phe Leu Leu Ile Phe Trp Met Ile Leu Phe Thr Ile  
                     145                    150                    155                    160  
 40 Pro Val Leu Val Leu Leu Ala Leu Gln Ser Asp Leu Gly Thr Ala Leu  
                     165                    170                    175  
 Val Phe Val Ala Ile Phe Ser Gly Ile Val Leu Leu Ser Gly Val Ser  
                     180                    185                    190  
 45 Trp Lys Ile Ile Ile Pro Val Phe Val Thr Ala Val Thr Gly Val Ala  
                     195                    200                    205  
 Gly Phe Leu Ala Ile Phe Ile Ser Lys Asp Gly Arg Ala Phe Leu His  
                     210                    215                    220  
 50 Gln Ile Gly Met Pro Thr Tyr Gln Ile Asn Arg Ile Leu Ala Trp Leu  
                     225                    230                    235                    240  
 55 Asn Pro Phe Glu Phe Ala Gln Thr Thr Thr Tyr Gln Gln Ala Gln Gly  
                     245                    250                    255  
 Gln Ile Ala Ile Gly Ser Gly Gly Leu Phe Gly Gln Gly Phe Asn Ala

95

Met Asp Ile Pro Leu Leu Phe Glu Gln Asp Tyr Ser Asp Trp Phe Ala  
 115 120 125

5 Glu Thr Trp Leu Val Tyr Val Asp Arg Asp Ala Gln Val Glu Arg Leu  
 130 135 140

Met Lys Arg Asp Gln Leu Ser Lys Asp Glu Ala Glu Ser Arg Met Ala  
 145 150 155 160

10 Ala Gln Trp Pro Leu Glu Lys Lys Lys Asp Leu Ala Ser Gln Val Leu  
 165 170 175

Asp Asn Asn Gly Asn Gln Asn Gln Leu Leu Asn Gln Val His Ile Leu  
 180 185 190

15 Leu Glu Gly Gly Arg Gln Asp Asp Arg Asp  
 195 200

20 <210> 156  
 <211> 419  
 <212> PRT  
 <213> Streptococcus pneumoniae

25 <400> 156  
 Met Arg Lys Ile Val Ile Asn Gly Gly Leu Pro Leu Gln Gly Glu Ile  
 1 5 10 15

30 Thr Ile Ser Gly Ala Lys Asn Ser Val Val Ala Leu Ile Pro Ala Ile  
 20 25 30

Ile Leu Ala Asp Asp Val Val Thr Leu Asp Cys Val Pro Asp Ile Ser  
 35 40 45

35 Asp Val Ala Ser Leu Val Glu Ile Met Glu Leu Met Gly Ala Thr Val  
 50 55 60

Lys Arg Tyr Asp Asp Val Leu Glu Ile Asp Pro Arg Gly Val Gln Asn  
 65 70 75 80

40 Ile Pro Met Pro Tyr Gly Lys Ile Asn Ser Leu Arg Ala Ser Tyr Tyr  
 85 90 95

45 Phe Tyr Gly Ser Leu Leu Gly Arg Phe Gly Glu Ala Thr Val Gly Leu  
 100 105 110

Pro Gly Gly Cys Asp Leu Gly Pro Arg Pro Ile Asp Leu His Leu Lys  
 115 120 125

50 Ala Phe Glu Ala Met Gly Ala Thr Ala Ser Tyr Glu Gly Asp Asn Met  
 130 135 140

Lys Leu Ser Ala Lys Asp Thr Gly Leu His Gly Ala Ser Ile Tyr Met  
 145 150 155 160

55 Asp Thr Val Ser Val Gly Ala Thr Ile Asn Thr Met Ile Ala Ala Val  
 165 170 175

Lys Ala Asn Gly Arg Thr Ile Ile Glu Asn Ala Ala Arg Glu Pro Glu  
 180 185 190  
 5 Ile Ile Asp Val Ala Thr Leu Leu Asn Asn Met Gly Ala His Ile Arg  
 195 200 205  
 Gly Ala Gly Thr Asn Ile Ile Ile Ile Asp Gly Val Glu Arg Leu His  
 210 215 220  
 10 Gly Thr Arg His Gln Val Ile Pro Asp Arg Ile Glu Ala Gly Thr Tyr  
 225 230 235 240  
 15 Ile Ser Leu Ala Ala Ala Val Gly Lys Gly Ile Arg Ile Asn Asn Val  
 245 250 255  
 Leu Tyr Glu His Leu Glu Gly Phe Ile Ala Lys Leu Glu Glu Met Gly  
 260 265 270  
 20 Val Arg Met Thr Val Ser Glu Asp Ser Ile Phe Val Glu Glu Gln Ser  
 275 280 285  
 Asn Leu Lys Ala Ile Asn Ile Lys Thr Ala Pro Tyr Pro Gly Phe Ala  
 290 295 300  
 25 Thr Asp Leu Gln Gln Pro Leu Thr Pro Leu Leu Leu Arg Ala Asn Gly  
 305 310 315 320  
 30 Arg Gly Thr Ile Val Asp Thr Ile Tyr Glu Lys Arg Val Asn His Val  
 325 330 335  
 Phe Glu Leu Ala Lys Met Asp Ala Asp Ile Ser Thr Thr Asn Gly His  
 340 345 350  
 35 Ile Leu Tyr Thr Gly Gly Arg Asp Leu Arg Gly Ala Ser Val Lys Ala  
 355 360 365  
 Thr Asp Leu Arg Ala Gly Ala Ala Leu Val Ile Ala Gly Leu Met Ala  
 370 375 380  
 40 Glu Gly Lys Thr Glu Ile Thr Asn Ile Glu Phe Ile Leu Arg Gly Tyr  
 385 390 395 400  
 45 Ser Asp Ile Ile Glu Lys Leu Arg Asn Leu Gly Ala Asp Ile Arg Leu  
 405 410 415  
 Val Glu Asp  
 50  
 <210> 157  
 <211> 231  
 <212> PRT  
 <213> Streptococcus pneumoniae  
 55  
 <400> 157  
 Met Ser Arg Ile Glu Phe Ser Pro Ser Leu Met Thr Met Asp Leu Asp

1                      5                      10                      15  
 Lys Phe Lys Glu Gln Ile Thr Phe Leu Asn Asp Lys Val Ala Ser Tyr  
                          20                      25                      30  
 5 His Ile Asp Ile Met Asp Gly His Phe Val Pro Asn Ile Thr Leu Ser  
                          35                      40                      45  
 10 Pro Trp Phe Ile Gln Glu Val Gln Lys Ile Ser Asp Thr Pro Leu Ser  
                          50                      55                      60  
 Val His Leu Met Val Thr Asp Pro Thr Phe Trp Val Asp Gln Val Leu  
                          65                      70                      75                      80  
 15 Asp Leu Gln Cys Glu Tyr Ile Cys Ile His Ala Glu Val Leu Asn Gly  
    85                      90                      95  
 Leu Ala Phe Arg Leu Ile Asp Lys Ile His Asp Ala Gly Leu Lys Ala  
    100                      105                      110  
 20 Gly Val Val Leu Asn Pro Glu Thr Pro Val Ser Thr Ile Phe Pro Tyr  
    115                      120                      125  
 25 Ile Asp Leu Leu Asp Lys Val Thr Ile Met Thr Val Asp Pro Gly Phe  
    130                      135                      140  
 Ala Gly Gln Arg Phe Leu Glu Ser Thr Leu Tyr Lys Ile Gln Glu Leu  
    145                      150                      155                      160  
 30 Arg Gln Leu Arg Val Gln Asn Gly Tyr His Tyr Ile Ile Glu Met Asp  
    165                      170                      175  
 Gly Ser Ser Ser Arg Lys Thr Phe Lys Gln Ile Asp Val Ala Gly Pro  
    180                      185                      190  
 35 Asp Ile Tyr Val Ile Gly Arg Ser Gly Leu Phe Gly Leu Asp Asp Asp  
    195                      200                      205  
 40 Ile Ala Lys Ala Trp Asp Ile Cys Ser Arg Asp Tyr Glu Glu Met Thr  
    210                      215                      220  
 Gly Lys Thr Met Pro Ile Lys  
    225                      230  
 45  
 <210> 158  
 <211> 374  
 <212> PRT  
 <213> Streptococcus pneumoniae  
 50  
 <400> 158  
 Met Arg Asn Met Ala Leu Thr Ala Gly Ile Val Gly Leu Pro Asn Val  
    1                      5                      10                      15  
 55 Gly Lys Ser Thr Leu Phe Asn Ala Ile Thr Lys Ala Gly Ala Glu Ala  
    20                      25                      30

Ala Asn Tyr Pro Phe Ala Thr Ile Asp Pro Asn Val Gly Met Val Glu  
           35                          40                          45  
 5 Asp Pro Asp Glu Arg Leu Gln Lys Leu Thr Glu Met Ile Thr Pro Lys  
       50                          55                          60  
 Lys Thr Val Pro Thr Thr Phe Glu Phe Thr Asp Ile Ala Gly Ile Val  
       65                          70                          75                          80  
 10 Lys Gly Ala Ser Lys Gly Glu Gly Leu Gly Asn Lys Phe Leu Ala Asn  
                           85                          90                          95  
 Ile Arg Glu Val Asp Ala Ile Val His Val Val Arg Ala Phe Asp Asp  
                           100                          105                          110  
 15 Glu Asn Val Met Arg Glu Gln Gly Arg Glu Asp Ala Phe Val Asp Pro  
                           115                          120                          125  
 20 Leu Ala Asp Ile Asp Thr Ile Asn Leu Glu Leu Ile Leu Ala Asp Leu  
                           130                          135                          140  
 Glu Ser Val Asn Lys Arg Tyr Ala Arg Val Glu Lys Met Ala Arg Thr  
       145                          150                          155                          160  
 25 Gln Lys Asp Lys Glu Ser Val Ala Glu Phe Asn Val Leu Gln Lys Ile  
                           165                          170                          175  
 Lys Pro Val Leu Glu Asp Gly Lys Ser Ala Arg Thr Ile Glu Phe Thr  
                           180                          185                          190  
 30 Asp Glu Glu Gln Lys Val Val Lys Gly Leu Phe Leu Leu Thr Thr Lys  
                           195                          200                          205  
 35 Pro Val Leu Tyr Val Ala Asn Val Asp Glu Asp Val Val Ser Glu Pro  
                           210                          215                          220  
 Asp Ser Ile Asp Tyr Val Lys Gln Ile Arg Glu Phe Ala Ala Thr Glu  
       225                          230                          235                          240  
 40 Asn Ala Glu Val Val Val Ile Ser Ala Arg Ala Glu Glu Glu Ile Ser  
                           245                          250                          255  
 Glu Leu Asp Asp Glu Asp Lys Lys Glu Phe Leu Glu Ala Ile Gly Leu  
                           260                          265                          270  
 45 Thr Glu Ser Gly Val Asp Lys Leu Thr Arg Ala Ala Tyr His Leu Leu  
                           275                          280                          285  
 50 Gly Leu Gly Thr Tyr Phe Thr Ala Gly Glu Lys Glu Val Arg Ala Trp  
                           290                          295                          300  
 Thr Phe Lys Arg Gly Met Lys Ala Pro Gln Ala Ala Gly Ile Ile His  
       305                          310                          315                          320  
 55 Ser Asp Phe Glu Lys Gly Phe Ile Arg Ala Val Thr Met Ser Tyr Glu  
                           325                          330                          335

Asp Leu Val Lys Tyr Gly Ser Glu Lys Ala Val Lys Glu Ala Gly Arg  
                   340                                  345                                  350

5 Leu Arg Glu Glu Gly Lys Glu Tyr Ile Val Gln Asp Gly Asp Ile Met  
                   355                                  360                                  365

Glu Phe Arg Phe Asn Val  
                   370

10 <210> 159  
       <211> 110  
       <212> PRT  
       <213> Streptococcus pneumoniae

15 <400> 159  
 Met Glu Ile Glu Lys Thr Asn Arg Met Asn Ala Leu Phe Glu Phe Tyr  
       1                                  5                                  10                                  15

20 Ala Ala Leu Leu Thr Asp Lys Gln Met Asn Tyr Ile Glu Leu Tyr Tyr  
                   20                                  25                                  30

Ala Asp Asp Tyr Ser Leu Ala Glu Ile Ala Glu Glu Phe Gly Val Ser  
                   35                                  40                                  45

25 Arg Gln Ala Val Tyr Asp Asn Ile Lys Arg Thr Glu Lys Ile Leu Glu  
                   50                                  55                                  60

30 Asp Tyr Glu Met Lys Leu His Met Tyr Ser Asp Tyr Ile Val Arg Ser  
                   65                                  70                                  75                                  80

Gln Ile Phe Asp Gln Ile Leu Glu Arg Tyr Pro Lys Asp Asp Phe Leu  
                                   85                                  90                                  95

35 Gln Glu Gln Ile Glu Ile Leu Thr Ser Ile Asp Asn Arg Glu  
                   100                                  105                                  110

40 <210> 160  
       <211> 223  
       <212> PRT  
       <213> Streptococcus pneumoniae

45 <400> 160  
 Met Thr Leu Glu Trp Glu Glu Phe Leu Asp Pro Tyr Ile Gln Ala Val  
       1                                  5                                  10                                  15

Gly Glu Leu Lys Ile Lys Leu Arg Gly Ile Arg Lys Gln Tyr Arg Lys  
                   20                                  25                                  30

50 Gln Asn Lys His Ser Pro Ile Glu Phe Val Thr Gly Arg Val Lys Pro  
                   35                                  40                                  45

55 Ile Glu Ser Ile Lys Glu Lys Met Ala Arg Arg Gly Ile Thr Tyr Ala  
                   50                                  55                                  60

Thr Leu Glu His Asp Leu Gln Asp Ile Ala Gly Leu Arg Val Met Val



101

Ser Leu Val Asp Leu Arg His Asp Pro Ser Ala Asp Asp Val Gln Met  
 115 120 125  
 5 Tyr Glu Phe Leu Lys Tyr Tyr Glu Ile Pro Val Ile Ile Val Ala Thr  
 130 135 140  
 Lys Ala Asp Lys Ile Pro Arg Gly Lys Trp Asn Lys His Glu Ser Ala  
 145 150 155 160  
 10 Ile Lys Lys Lys Leu Asn Phe Asp Pro Ser Asp Asp Phe Ile Leu Phe  
 165 170 175  
 Ser Ser Val Ser Lys Ala Gly Met Asp Glu Ala Trp Asp Ala Ile Leu  
 180 185 190  
 15 Glu Lys Leu  
 195  
 20 <210> 162  
 <211> 97  
 <212> PRT  
 <213> Streptococcus pneumoniae  
 25 <400> 162  
 Met Lys Thr Arg Lys Ile Pro Leu Arg Lys Ser Val Val Ser Asn Glu  
 1 5 10 15  
 30 Val Ile Asp Lys Arg Asp Leu Leu Arg Ile Val Lys Asn Lys Glu Gly  
 20 25 30  
 Gln Val Phe Ile Asp Pro Thr Gly Lys Ala Asn Gly Arg Gly Ala Tyr  
 35 40 45  
 35 Ile Lys Leu Asp Asn Ala Glu Ala Leu Glu Ala Lys Lys Lys Lys Val  
 50 55 60  
 Phe Asn Arg Ser Phe Ser Met Glu Val Glu Glu Ser Phe Tyr Asp Glu  
 65 70 75 80  
 40 Leu Ile Ala Tyr Val Asp His Lys Val Lys Arg Arg Glu Leu Gly Leu  
 85 90 95  
 Glu  
 45  
 <210> 163  
 <211> 103  
 50 <212> PRT  
 <213> Streptococcus pneumoniae  
 <400> 163  
 Met Leu Lys Pro Ser Ile Asp Thr Leu Leu Asp Lys Val Pro Ser Lys  
 55 1 5 10 15  
 Tyr Ser Leu Val Ile Leu Glu Ala Lys Arg Ala His Glu Leu Glu Ala

20 25 30

5 Gly Ala Pro Ala Thr Gln Gly Phe Lys Ser Glu Lys Ser Thr Leu Arg  
35 40 45

Ala Leu Glu Glu Ile Glu Ser Gly Asn Val Thr Ile His Pro Asp Pro  
50 55 60

10 Glu Gly Lys Arg Glu Ala Val Arg Arg Arg Ile Glu Glu Glu Lys Arg  
65 70 75 80

Arg Lys Glu Glu Glu Glu Lys Lys Ile Lys Glu Gln Ile Ala Lys Glu  
85 90 95

15 Lys Glu Asp Gly Glu Lys Ile  
100

20 <210> 164  
<211> 103  
<212> PRT  
<213> Streptococcus pneumoniae

25 <400> 164  
Met Ser Leu Thr Ser Lys Gln Arg Ala Phe Leu Asn Ser Gln Ala His  
1 5 10 15

Thr Leu Lys Pro Ile Ile Gln Ile Gly Lys Asn Gly Leu Asn Asp Gln  
20 25 30

30 Ile Lys Thr Ser Val Arg Gln Ala Leu Asp Ala Arg Glu Leu Ile Lys  
35 40 45

35 Val Thr Leu Leu Gln Asn Thr Asp Glu Asn Ile His Glu Val Ala Glu  
50 55 60

Ile Leu Glu Glu Glu Ile Gly Val Asp Thr Val Gln Lys Ile Gly Arg  
65 70 75 80

40 Ile Leu Ile Leu Phe Lys Gln Ser Ser Lys Lys Glu Asn Arg Lys Ile  
85 90 95

Ser Lys Lys Val Lys Glu Ile  
100

45 <210> 165  
<211> 175  
<212> PRT  
<213> Streptococcus pneumoniae

50 <400> 165  
Met Ala Ile Glu Asn Tyr Ile Pro Asp Phe Ala Val Glu Ala Val Tyr  
1 5 10 15

Asp Leu Thr Val Pro Ser Leu Gln Ala Gln Gly Ile Lys Ala Val Leu  
20 25 30

Val Asp Leu Asp Asn Thr Leu Ile Ala Trp Asn Asn Pro Asp Gly Thr  
 35 40 45  
 5 Pro Glu Met Lys Gln Trp Leu His Asp Leu Arg Asp Ala Gly Ile Gly  
 50 55 60  
 Ile Ile Val Val Ser Asn Asn Thr Lys Lys Arg Val Gln Arg Ala Val  
 65 70 75 80  
 10 Glu Lys Phe Gly Ile Asp Tyr Val Tyr Trp Ala Leu Lys Pro Phe Thr  
 85 90 95  
 Phe Gly Ile Asp Arg Ala Met Lys Glu Phe His Tyr Asp Lys Lys Glu  
 100 105 110  
 15 Val Val Met Val Gly Asp Gln Leu Met Thr Asp Ile Arg Ala Ala His  
 115 120 125  
 20 Arg Ala Gly Ile Arg Ser Ile Leu Val Lys Pro Leu Val Gln His Asp  
 130 135 140  
 Ser Ile Lys Thr Gln Ile Asn Arg Thr Arg Glu Arg Arg Val Met Arg  
 145 150 155 160  
 25 Lys Ile Thr Glu Lys Tyr Gly Pro Ile Thr Tyr Lys Lys Gly Ile  
 165 170 175  
 30 <210> 166  
 <211> 455  
 <212> PRT  
 <213> Streptococcus pneumoniae  
 35 <400> 166  
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 40 Ile Ile Arg Ala Ala Arg Glu Leu Gly Ile Ala Thr Val Ala Val Tyr  
 20 25 30  
 Ser Thr Ala Asp Lys Glu Ala Leu His Thr Leu Leu Ala Asp Glu Ala  
 35 40 45  
 45 Val Cys Ile Gly Pro Gly Lys Ala Thr Glu Ser Tyr Leu Asn Ile Asn  
 50 55 60  
 Ala Val Leu Ser Ala Ala Val Leu Thr Glu Ala Glu Ala Ile His Pro  
 65 70 75 80  
 50 Gly Phe Gly Phe Leu Ser Glu Asn Ser Lys Phe Ala Thr Met Cys Glu  
 85 90 95  
 55 Glu Ile Gly Ile Lys Phe Ile Gly Pro Ser Gly His Val Met Asp Met  
 100 105 110  
 Met Gly Asp Lys Ile Asn Ala Arg Ala Gln Met Ile Lys Ala Gly Val

	115	120	125
	Pro Val Ile Pro Gly Ser Asp Gly Glu Val His Asn Ser Glu Glu Ala		
	130	135	140
5	Leu Ile Val Ala Glu Lys Ile Gly Tyr Pro Val Met Leu Lys Ala Ser		
	145	150	155 160
10	Ala Gly Gly Gly Gly Lys Gly Ile Arg Lys Val Glu Lys Pro Asp Asp		
	165	170	175
	Leu Val Ser Ala Phe Glu Thr Ala Ser Ser Glu Ala Lys Ala Asn Tyr		
	180	185	190
15	Gly Asn Gly Ala Met Tyr Ile Glu Arg Val Ile Tyr Pro Ala Arg His		
	195	200	205
	Ile Glu Val Gln Ile Leu Gly Asp Glu His Gly His Val Ile His Leu		
20	210	215	220
	Gly Glu Arg Asp Cys Ser Leu Gln Arg Asn Asn Gln Lys Val Leu Glu		
	225	230	235 240
25	Glu Ser Pro Ser Ile Ala Ile Gly Lys Thr Leu Arg His Glu Ile Gly		
	245	250	255
	Ala Ala Ala Val Arg Ala Ala Glu Phe Val Gly Tyr Glu Asn Ala Gly		
	260	265	270
30	Thr Ile Glu Phe Leu Leu Asp Glu Ala Ser Ser Asn Phe Tyr Phe Met		
	275	280	285
	Glu Met Asn Thr Arg Val Gln Val Glu His Pro Val Thr Glu Phe Val		
35	290	295	300
	Ser Gly Val Asp Ile Val Lys Glu Gln Ile Cys Ile Ala Ala Gly Gln		
	305	310	315 320
40	Pro Leu Ser Val Lys Gln Glu Asp Ile Val Leu Arg Gly His Ala Ile		
	325	330	335
	Glu Cys Arg Ile Asn Ala Glu Asn Pro Ala Phe Asn Phe Ala Pro Ser		
	340	345	350
45	Pro Gly Lys Ile Thr Asn Leu Tyr Leu Pro Ser Gly Gly Val Gly Leu		
	355	360	365
	Arg Val Asp Ser Ala Val Tyr Pro Gly Tyr Thr Ile Pro Pro Tyr Tyr		
50	370	375	380
	Asp Ser Met Ile Ala Lys Ile Ile Val His Gly Glu Asn Arg Phe Asp		
	385	390	395 400
55	Ala Leu Met Lys Met Gln Arg Ala Leu Tyr Glu Leu Glu Ile Glu Gly		
	405	410	415
	Val Gln Thr Asn Ala Asp Phe Gln Leu Asp Leu Ile Ser Asp Arg Asn		

420 425 430  
 Val Ile Ala Gly Asp Tyr Asp Thr Cys Phe Leu Met Glu Thr Phe Leu  
 435 440 445  
 5 Pro Lys Tyr Gln Glu Lys Glu  
 450 455  
 10 <210> 167  
 <211> 77  
 <212> PRT  
 <213> Streptococcus pneumoniae  
 15 <400> 167  
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 20 Arg Glu Thr Thr Arg Ala Leu Tyr Leu Asp Ile Asp Thr Ser Ser Glu  
 20 25 30  
 Leu Glu Gly Arg Ile Thr Ala Arg Gln Leu Val Glu Glu Asn Arg Pro  
 35 40 45  
 25 Glu Tyr Asn Ile Glu Tyr Ile Glu Leu Leu Ser Asp Lys Leu Leu Asp  
 50 55 60  
 Tyr Glu Lys Glu Thr Gly Ala Phe Glu Ile Thr Glu Phe  
 65 70 75  
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 <210> 168  
 <211> 336  
 <212> PRT  
 35 <213> Streptococcus pneumoniae  
 <400> 168  
 Met Lys Asp Arg Tyr Ile Leu Ala Phe Glu Thr Ser Cys Asp Glu Thr  
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 40 Ser Val Ala Val Leu Lys Asn Asp Asp Glu Leu Leu Ser Asn Val Ile  
 20 25 30  
 45 Ala Ser Gln Ile Glu Ser His Lys Arg Phe Gly Gly Val Val Pro Glu  
 35 40 45  
 Val Ala Ser Arg His His Val Glu Val Ile Thr Ala Cys Ile Glu Glu  
 50 55 60  
 50 Ala Leu Ala Glu Ala Gly Ile Thr Glu Glu Asp Val Thr Ala Val Ala  
 65 70 75 80  
 Val Thr Tyr Gly Pro Gly Leu Val Gly Ala Leu Leu Val Gly Leu Ser  
 85 90 95  
 55 Ala Ala Lys Ala Phe Ala Trp Ala His Gly Leu Pro Leu Ile Pro Val  
 100 105 110

Asn His Met Ala Gly His Leu Met Ala Ala Gln Ser Val Glu Pro Leu  
 115 120 125  
 5 Glu Phe Pro Leu Leu Ala Leu Leu Val Ser Gly Gly His Thr Glu Leu  
 130 135 140  
 Val Tyr Val Ser Glu Ala Gly Asp Tyr Lys Ile Val Gly Glu Thr Arg  
 145 150 155 160  
 10 Asp Asp Ala Val Gly Glu Ala Tyr Asp Lys Val Gly Arg Val Met Gly  
 165 170 175  
 Leu Thr Tyr Pro Ala Gly Arg Glu Ile Asp Glu Leu Ala His Gln Gly  
 180 185 190  
 15 Gln Asp Ile Tyr Asp Phe Pro Arg Ala Met Ile Lys Glu Asp Asn Leu  
 195 200 205  
 20 Glu Phe Ser Phe Ser Gly Leu Lys Ser Ala Phe Ile Asn Leu His His  
 210 215 220  
 Asn Ala Glu Gln Lys Gly Glu Ser Leu Ser Thr Glu Asp Leu Cys Ala  
 225 230 235 240  
 25 Ser Phe Gln Ala Ala Val Met Asp Ile Leu Met Ala Lys Thr Lys Lys  
 245 250 255  
 Ala Leu Glu Glu Tyr Pro Val Lys Thr Leu Phe Val Ala Gly Gly Val  
 260 265 270  
 30 Ala Ala Asn Lys Gly Leu Arg Glu Arg Leu Ala Ala Glu Ile Thr Asp  
 275 280 285  
 35 Val Lys Val Ile Ile Pro Pro Leu Arg Leu Cys Gly Asp Asn Ala Gly  
 290 295 300  
 Met Ile Ala Tyr Ala Ser Val Ser Glu Trp Asn Lys Glu Asn Phe Ala  
 305 310 315 320  
 40 Gly Trp Asp Leu Asn Ala Lys Pro Ser Leu Ala Phe Asp Thr Met Glu  
 325 330 335  
 45  
 <210> 169  
 <211> 602  
 50 <212> PRT  
 <213> Streptococcus pneumoniae  
 <400> 169  
 Met Cys Gly Ile Val Gly Val Val Gly Asn Thr Asn Ala Thr Asp Ile  
 55 1 5 10 15  
 Leu Ile Gln Gly Leu Glu Lys Leu Glu Tyr Arg Gly Tyr Asp Ser Ala

20 25 30  
 Gly Ile Phe Val Leu Asp Gly Ala Asp Asn His Leu Val Lys Ala Val  
 35 40 45  
 5 Gly Arg Ile Ala Glu Leu Ser Ala Lys Thr Ala Gly Val Glu Gly Thr  
 50 55 60  
 10 Thr Gly Ile Gly His Thr Arg Trp Ala Thr His Gly Lys Pro Thr Glu  
 65 70 75 80  
 Asp Asn Ala His Pro His Arg Ser Glu Thr Glu Arg Phe Val Leu Val  
 85 90 95  
 15 His Asn Gly Val Ile Glu Asn Tyr Leu Glu Ile Lys Glu Glu Tyr Leu  
 100 105 110  
 Ala Gly His His Phe Lys Gly Gln Thr Asp Thr Glu Ile Ala Val His  
 115 120 125  
 20 Leu Ile Gly Lys Phe Ala Glu Glu Glu Gly Leu Ser Val Leu Glu Ala  
 130 135 140  
 Phe Lys Lys Ala Leu His Ile Ile Arg Gly Ser Tyr Ala Phe Ala Leu  
 145 150 155 160  
 Ile Asp Ser Glu Asn Pro Asp Val Ile Tyr Val Ala Lys Asn Lys Ser  
 165 170 175  
 30 Pro Leu Leu Ile Gly Leu Gly Glu Gly Tyr Asn Met Val Cys Ser Asp  
 180 185 190  
 Ala Met Ala Met Ile Arg Glu Thr Asn Gln Tyr Met Glu Ile His Asp  
 195 200 205  
 35 Gln Glu Leu Val Ile Val Lys Ala Asp Ser Val Glu Val Gln Asp Tyr  
 210 215 220  
 Asp Gly Asn Ser Arg Glu Arg Ala Ser Tyr Thr Ala Glu Leu Asp Leu  
 225 230 235 240  
 Ser Asp Ile Gly Lys Gly Thr Tyr Pro Tyr Tyr Met Leu Lys Glu Ile  
 245 250 255  
 45 Asp Glu Gln Pro Thr Val Met Arg Lys Leu Ile Gln Ala Tyr Thr Asp  
 260 265 270  
 Asp Ala Gly Gln Val Val Val Ala Pro Ala Ile Ile Lys Ala Val Gln  
 275 280 285  
 50 Asp Ala Asp Arg Ile Tyr Ile Leu Ala Ala Gly Thr Ser Tyr His Ala  
 290 295 300  
 Gly Phe Ala Ser Lys Lys Met Leu Glu Glu Leu Thr Asp Thr Pro Val  
 305 310 315 320  
 55 Glu Leu Gly Ile Ser Ser Glu Trp Gly Tyr Gly Met Pro Leu Leu Ser



	325	330	335
	Lys Lys Pro Leu Phe Ile Phe Ile Ser Gln Ser Gly Glu Thr Ala Asp		
	340	345	350
5	Ser Arg Gln Val Leu Val Lys Ala Asn Glu Met Gly Ile Pro Ser Leu		
	355	360	365
10	Thr Val Thr Asn Val Pro Gly Ser Thr Leu Ser Arg Glu Ala Asn Tyr		
	370	375	380
	Thr Met Leu Leu His Ala Gly Pro Glu Ile Ala Val Ala Ser Thr Lys		
	385	390	395
15	Ala Tyr Thr Ala Gln Ile Ala Ala Leu Ala Phe Leu Ala Lys Ala Val		
	405	410	415
	Gly Glu Ala Asn Gly Asn Ala Lys Ala Gln Ala Phe Asp Leu Val His		
	420	425	430
20	Glu Leu Ser Ile Val Ala Gln Ser Ile Glu Ser Thr Leu Ser Glu Lys		
	435	440	445
	Glu Thr Ile Glu Ala Lys Val Arg Glu Leu Leu Glu Thr Thr Arg Asn		
25	450	455	460
	Ala Phe Tyr Ile Gly Arg Gly Gln Asp Tyr Tyr Val Ala Met Glu Ala		
	465	470	475
30	Ser Leu Lys Leu Lys Glu Ile Ser Tyr Ile Gln Cys Glu Gly Phe Ala		
	485	490	495
	Ala Gly Glu Leu Lys His Gly Thr Ile Ala Leu Ile Glu Glu Gly Thr		
	500	505	510
35	Pro Val Leu Ala Leu Leu Ser Asp Pro Val Leu Ala Asn His Thr Arg		
	515	520	525
	Gly Asn Ile Gln Glu Val Ala Ala Arg Gly Ala Lys Val Leu Thr Ile		
40	530	535	540
	Ala Glu Glu Asn Val Ala Lys Asp Thr Asp Asp Ile Val Leu Thr Thr		
	545	550	555
45	Val His Pro Tyr Leu Ser Pro Ile Ser Met Val Val Pro Thr Gln Leu		
	565	570	575
	Val Ala Tyr Phe Ala Thr Leu His Arg Gly Leu Asp Val Asp Lys Pro		
	580	585	590
50	Arg Asn Leu Ala Lys Ser Val Thr Val Glu		
	595	600	
55	<210> 170		
	<211> 240		
	<212> PRT		

<213> Streptococcus pneumoniae

<400> 170

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1 5 10 15  
Leu Lys Asp Ile Ser Leu Val Leu His Gly Pro Thr Ile Thr Gly Ile  
20 25 30  
10 Ile Gly Pro Asn Gly Ala Gly Lys Ser Thr Leu Leu Lys Gly Met Leu  
35 40 45  
Gly Ile Ile Pro His Gln Gly Gln Ala Phe Leu Asp Asp Lys Glu Val  
50 55 60  
15 Lys Lys Ser Leu His Arg Ile Ala Tyr Val Glu Gln Lys Ile Asn Ile  
65 70 75 80  
20 Asp Tyr Asn Phe Pro Ile Lys Val Lys Glu Cys Val Ser Leu Gly Leu  
85 90 95  
Phe Pro Ser Ile Pro Leu Phe Arg Ser Leu Lys Ala Lys His Trp Lys  
100 105 110  
25 Lys Val Gln Glu Ala Leu Glu Ile Val Gly Leu Ala Asp Tyr Ala Glu  
115 120 125  
Arg Gln Ile Ser Gln Leu Ser Gly Gly Gln Phe Gln Arg Val Leu Ile  
130 135 140  
30 Ala Arg Cys Leu Val Gln Glu Ala Asp Tyr Ile Leu Leu Asp Glu Pro  
145 150 155 160  
35 Phe Ala Gly Ile Asp Ser Val Ser Glu Glu Ile Ile Met Asn Thr Leu  
165 170 175  
Arg Asp Leu Lys Lys Ala Gly Lys Thr Val Leu Ile Val His His Asp  
180 185 190  
40 Leu Ser Lys Ile Pro His Tyr Phe Asp Gln Val Leu Leu Val Asn Arg  
195 200 205  
Glu Val Ile Ala Phe Gly Pro Thr Lys Glu Thr Phe Thr Glu Thr Asn  
210 215 220  
45 Leu Lys Glu Ala Tyr Gly Asn Gln Leu Phe Phe Asn Gly Gly Asp Leu  
225 230 235 240

50

<210> 171

<211> 740

55 <212> PRT

<213> Streptococcus pneumoniae

<400> 171  
 Met Pro Lys Glu Val Asn Leu Thr Gly Glu Glu Val Val Ala Leu Thr  
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 5 Lys Glu Tyr Leu Thr Glu Glu Asp Val His Phe Val His Lys Ala Leu  
 20 25 30  
 Val Tyr Ala Val Glu Cys His Ser Gly Gln Tyr Arg Lys Ser Gly Glu  
 35 40 45  
 10 Pro Tyr Ile Ile His Pro Ile Gln Val Ala Gly Ile Leu Ala Lys Leu  
 50 55 60  
 15 Lys Leu Asp Ala Val Thr Val Ala Cys Gly Phe Leu His Asp Val Val  
 65 70 75 80  
 Glu Asp Thr Asp Ala Thr Leu Asp Asp Leu Glu Arg Glu Phe Gly Pro  
 85 90 95  
 20 Asp Val Arg Val Ile Val Asp Gly Val Thr Lys Leu Gly Lys Val Glu  
 100 105 110  
 Tyr Lys Ser Ile Glu Glu Gln Leu Ala Glu Asn His Arg Lys Met Leu  
 115 120 125  
 25 Met Ala Met Ser Glu Asp Ile Arg Val Ile Leu Val Lys Leu Ser Asp  
 130 135 140  
 30 Arg Leu His Asn Met Arg Thr Leu Lys His Leu Arg Lys Asp Lys Gln  
 145 150 155 160  
 Glu Arg Ile Ser Lys Glu Thr Met Glu Ile Tyr Ala Pro Leu Ala His  
 165 170 175  
 35 Arg Leu Gly Ile Ser Ser Val Lys Trp Glu Leu Glu Asp Leu Ser Phe  
 180 185 190  
 Arg Tyr Leu Asn Pro Thr Glu Phe Tyr Lys Ile Thr His Met Met Lys  
 195 200 205  
 40 Glu Lys Arg Arg Glu Arg Glu Ala Leu Val Asp Glu Val Val Thr Lys  
 210 215 220  
 45 Leu Glu Glu Tyr Thr Thr Glu Arg His Leu Lys Gly Lys Ile Tyr Gly  
 225 230 235 240  
 Arg Pro Lys His Ile Tyr Ser Ile Phe Arg Lys Met Gln Asp Lys Arg  
 245 250 255  
 50 Lys Arg Phe Glu Glu Ile Tyr Asp Leu Ile Ala Ile Arg Cys Ile Leu  
 260 265 270  
 Asp Thr Gln Ser Asp Val Tyr Ala Met Leu Gly Tyr Val His Glu Phe  
 275 280 285  
 55 Trp Lys Pro Met Pro Gly Arg Phe Lys Asp Tyr Ile Ala Asn Arg Lys  
 290 295 300

Ala Asn Gly Tyr Gln Ser Ile His Thr Thr Val Tyr Gly Pro Lys Gly  
 305 310 315 320  
 5 Pro Ile Glu Phe Gln Ile Arg Thr Lys Glu Met His Glu Val Ala Glu  
 325 330 335  
 Tyr Gly Val Ala Ala His Trp Ala Tyr Lys Lys Gly Ile Lys Gly Gln  
 340 345 350  
 10 Val Asn Ser Lys Glu Ser Ala Ile Gly Met Asn Trp Ile Lys Glu Met  
 355 360 365  
 15 Met Glu Leu Gln Asp Gln Ala Asp Asp Ala Lys Glu Phe Val Asp Ser  
 370 375 380  
 Val Lys Glu Asn Tyr Leu Ala Glu Glu Ile Tyr Val Phe Thr Pro Asp  
 385 390 395 400  
 20 Gly Ala Val Arg Ser Leu Pro Lys Asp Ser Gly Pro Ile Asp Phe Ala  
 405 410 415  
 Tyr Glu Ile His Thr Lys Val Gly Glu Lys Ala Thr Gly Ala Lys Val  
 420 425 430  
 25 Asn Gly Arg Met Val Pro Leu Thr Thr Lys Leu Lys Thr Gly Asp Gln  
 435 440 445  
 30 Val Glu Ile Ile Ala Asn Pro Asn Ser Phe Gly Pro Ser Arg Asp Trp  
 450 455 460  
 Leu Asn Met Val Lys Thr Ser Lys Ala Arg Asn Lys Ile Arg Gln Phe  
 465 470 475 480  
 35 Phe Lys Asn Gln Asp Lys Glu Leu Ser Val Asn Lys Gly Arg Glu Met  
 485 490 495  
 Leu Met Ala Gln Phe Gln Glu Asn Gly Tyr Val Ala Asn Lys Phe Met  
 500 505 510  
 40 Asp Lys Arg His Met Asp Gln Val Leu Gln Lys Thr Ser Tyr Lys Thr  
 515 520 525  
 45 Glu Asp Ser Leu Phe Ala Ala Ile Gly Phe Gly Glu Ile Gly Ala Ile  
 530 535 540  
 Thr Val Phe Asn Arg Leu Thr Glu Lys Glu Arg Arg Glu Glu Glu Arg  
 545 550 555 560  
 50 Ala Lys Ala Lys Ala Glu Ala Glu Glu Leu Val Lys Gly Gly Glu Val  
 565 570 575  
 Lys Val Glu Asn Lys Glu Thr Leu Lys Val Lys His Glu Gly Gly Val  
 580 585 590  
 55 Val Ile Glu Gly Ala Ser Gly Leu Leu Val Arg Ile Ala Lys Cys Cys  
 595 600 605

Asn Pro Val Pro Gly Asp Asp Ile Val Gly Tyr Ile Thr Lys Gly Arg  
 610 615 620  
 5 Gly Val Ala Ile His Arg Val Asp Cys Met Asn Leu Arg Ala Gln Glu  
 625 630 635 640  
 Asn Tyr Glu Gln Arg Leu Leu Asp Val Glu Trp Glu Asp Gln Tyr Ser  
 645 650 655  
 10 Ser Ser Asn Lys Glu Tyr Leu Ala His Ile Asp Ile Tyr Gly Leu Asn  
 660 665 670  
 Arg Thr Gly Leu Leu Asn Asp Val Leu Gln Val Leu Ser Asn Thr Thr  
 675 680 685  
 15 Lys Asn Ile Ser Thr Val Asn Ala Gln Pro Thr Lys Asp Met Lys Phe  
 690 695 700  
 20 Ala Asn Ile His Val Ser Phe Gly Ile Ala Asn Leu Ser Thr Leu Thr  
 705 710 715 720  
 Thr Val Val Asp Lys Ile Lys Ser Val Pro Glu Val Tyr Ser Val Lys  
 725 730 735  
 25 Arg Thr Asn Gly  
 740  
 30 <210> 172  
 <211> 492  
 <212> PRT  
 <213> Streptococcus pneumoniae  
 35 <400> 172  
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 40 Asp Val Leu Leu Ile Pro Ala Glu Ser His Val Leu Pro Asn Asp Ala  
 20 25 30  
 Asp Leu Thr Thr Lys Leu Ala Asp Asn Leu Thr Leu Asn Ile Pro Ile  
 35 40 45  
 45 Ile Thr Ala Ala Met Asp Thr Val Thr Glu Ser Gln Met Ala Ile Ala  
 50 55 60  
 Ile Ala Arg Ala Gly Gly Leu Gly Val Ile His Lys Asn Met Ser Ile  
 65 70 75 80  
 50 Ala Gln Gln Ala Asp Glu Val Arg Lys Val Lys Arg Ser Glu Asn Gly  
 85 90 95  
 55 Val Ile Ile Asp Pro Phe Phe Leu Thr Pro Glu His Thr Ile Ala Glu  
 100 105 110  
 Ala Asp Glu Leu Met Gly Arg Tyr Arg Ile Ser Gly Val Pro Val Val

	115	120	125
	Glu Thr Leu Glu Asn Arg Lys Leu Val Gly Ile Leu Thr Asn Arg Asp		
	130	135	140
5	Leu Arg Phe Ile Ser Asp Tyr Asn Gln Pro Ile Ser Asn His Met Thr		
	145	150	155 160
10	Ser Glu Asn Leu Val Thr Ala Pro Val Gly Thr Asp Leu Ala Thr Ala		
	165	170	175
	Glu Ser Ile Leu Gln Glu His Arg Ile Glu Lys Leu Pro Leu Val Asp		
	180	185	190
15	Glu Glu Gly Ser Leu Ser Gly Leu Ile Thr Ile Lys Asp Ile Glu Lys		
	195	200	205
	Val Ile Glu Phe Pro Asn Ala Ala Lys Asp Glu Phe Gly Arg Leu Leu		
	210	215	220
20	Val Ala Gly Ala Val Gly Val Thr Ser Asp Thr Phe Glu Arg Ala Glu		
	225	230	235 240
	Ala Leu Phe Glu Ala Gly Ala Asp Ala Ile Val Ile Asp Thr Ala His		
	245	250	255
25	Gly His Ser Ala Gly Val Leu Arg Lys Ile Ala Glu Ile Arg Ala His		
	260	265	270
30	Phe Pro Asp Arg Thr Leu Ile Ala Gly Asn Ile Ala Thr Ala Glu Gly		
	275	280	285
	Ala Arg Ala Leu Tyr Glu Ala Gly Val Asp Val Val Lys Val Gly Ile		
	290	295	300
35	Gly Pro Gly Ser Ile Cys Thr Thr Arg Val Ile Ala Gly Val Gly Val		
	305	310	315 320
40	Pro Gln Val Thr Ala Ile Tyr Asp Ala Ala Ala Val Ala Arg Glu Tyr		
	325	330	335
	Gly Lys Thr Ile Ile Ala Asp Gly Gly Ile Lys Tyr Ser Gly Asp Ile		
	340	345	350
45	Val Lys Ala Leu Ala Ala Gly Gly Asn Ala Val Met Leu Gly Ser Met		
	355	360	365
	Phe Ala Gly Thr Asp Glu Ala Pro Gly Glu Thr Glu Ile Phe Gln Gly		
	370	375	380
50	Arg Lys Phe Lys Thr Tyr Arg Gly Met Gly Ser Ile Ala Ala Met Lys		
	385	390	395 400
55	Lys Gly Ser Ser Asp Arg Tyr Phe Gln Gly Ser Val Asn Glu Ala Asn		
	405	410	415
	Lys Leu Val Pro Glu Gly Ile Glu Gly Arg Val Ala Tyr Lys Gly Ala		

420                      425                      430  
 Ala Ala Asp Ile Val Phe Gln Met Ile Gly Gly Ile Arg Ser Gly Met  
                     435                      440                      445  
 5 Gly Tyr Cys Gly Ala Ala Asn Leu Lys Glu Leu His Asp Asn Ala Gln  
                     450                      455                      460  
 10 Phe Ile Glu Met Ser Gly Ala Gly Leu Lys Glu Ser His Pro His Asp  
      465                      470                      475                      480  
 Val Gln Ile Thr Asn Glu Ala Pro Asn Tyr Ser Met  
                     485                      490  
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     <210> 173  
     <211> 648  
     <212> PRT  
     <213> Streptococcus pneumoniae  
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     <400> 173  
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                     20                      25                      30  
 Met Tyr Ile Gly Ser Thr Ser Lys Glu Gly Leu His His Leu Val Trp  
                     35                      40                      45  
 30 Glu Ile Val Asp Asn Ser Ile Asp Glu Ala Leu Ala Gly Phe Ala Ser  
      50                      55                      60  
 35 His Ile Gln Val Phe Ile Glu Pro Asp Asp Ser Ile Thr Val Val Asp  
      65                      70                      75                      80  
 Asp Gly Arg Gly Ile Pro Val Asp Ile Gln Glu Lys Thr Gly Arg Pro  
                     85                      90                      95  
 40 Ala Val Glu Thr Val Phe Thr Val Leu His Ala Gly Gly Lys Phe Gly  
                     100                      105                      110  
 Gly Gly Gly Tyr Lys Val Ser Gly Gly Leu His Gly Val Gly Ser Ser  
      115                      120                      125  
 45 Val Val Asn Ala Leu Ser Thr Gln Leu Asp Val His Val His Lys Asn  
      130                      135                      140  
 50 Gly Lys Ile His Tyr Gln Glu Tyr Arg Arg Gly His Val Val Ala Asp  
      145                      150                      155                      160  
 Leu Glu Ile Val Gly Asp Thr Asp Lys Thr Gly Thr Thr Val His Phe  
                     165                      170                      175  
 55 Thr Pro Asp Pro Lys Ile Phe Thr Glu Thr Thr Ile Phe Asp Phe Asp  
                     180                      185                      190

Lys Leu Asn Lys Arg Ile Gln Glu Leu Ala Phe Leu Asn Arg Gly Leu  
 195 200 205  
 5 Gln Ile Ser Ile Thr Asp Lys Arg Gln Gly Leu Glu Gln Thr Lys His  
 210 215 220  
 Tyr His Tyr Glu Gly Gly Ile Ala Ser Tyr Val Glu Tyr Ile Asn Glu  
 225 230 235 240  
 10 Asn Lys Asp Val Ile Phe Asp Thr Pro Ile Tyr Thr Asp Gly Glu Met  
 245 250 255  
 Asp Asp Ile Thr Val Glu Val Ala Met Gln Tyr Thr Thr Gly Tyr His  
 260 265 270  
 15 Glu Asn Val Met Ser Phe Ala Asn Asn Ile His Thr His Glu Gly Gly  
 275 280 285  
 20 Thr His Glu Gln Gly Phe Arg Thr Ala Leu Thr Arg Val Ile Asn Asp  
 290 295 300  
 Tyr Ala Arg Lys Asn Lys Leu Leu Lys Asp Asn Glu Asp Asn Leu Thr  
 305 310 315 320  
 25 Gly Glu Asp Val Arg Glu Gly Leu Thr Ala Val Ile Ser Val Lys His  
 325 330 335  
 Pro Asn Pro Gln Phe Glu Gly Gln Thr Lys Thr Lys Leu Gly Asn Ser  
 340 345 350  
 30 Glu Val Val Lys Ile Thr Asn Arg Leu Phe Ser Glu Ala Phe Ser Asp  
 355 360 365  
 35 Phe Leu Met Glu Asn Pro Gln Ile Ala Lys Arg Ile Val Glu Lys Gly  
 370 375 380  
 Ile Leu Ala Ala Lys Ala Arg Val Ala Ala Lys Arg Ala Arg Glu Val  
 385 390 395 400  
 40 Thr Arg Lys Lys Ser Gly Leu Glu Ile Ser Asn Leu Pro Gly Lys Leu  
 405 410 415  
 Ala Asp Cys Ser Ser Asn Asn Pro Ala Glu Thr Glu Leu Phe Ile Val  
 420 425 430  
 45 Glu Gly Asp Ser Ala Gly Gly Ser Ala Lys Ser Gly Arg Asn Arg Glu  
 435 440 445  
 50 Phe Gln Ala Ile Leu Pro Ile Arg Gly Lys Ile Leu Asn Val Glu Lys  
 450 455 460  
 Ala Ser Met Asp Lys Ile Leu Ala Asn Glu Glu Ile Arg Ser Leu Phe  
 465 470 475 480  
 55 Thr Ala Met Gly Thr Gly Phe Gly Ala Glu Phe Asp Val Ser Lys Ala  
 485 490 495



Arg Tyr Gln Lys Leu Val Leu Met Thr Asp Ala Asp Val Asp Gly Ala  
 500 505 510  
 5 His Ile Arg Thr Leu Leu Leu Thr Leu Ile Tyr Arg Tyr Met Lys Pro  
 515 520 525  
 Ile Leu Glu Ala Gly Tyr Val Tyr Ile Ala Gln Pro Pro Ile Tyr Gly  
 530 535 540  
 10 Val Lys Val Gly Ser Glu Ile Lys Glu Tyr Ile Gln Pro Gly Ala Asp  
 545 550 555 560  
 Gln Glu Ile Lys Leu Gln Glu Ala Leu Ala Arg Tyr Ser Glu Gly Arg  
 565 570 575  
 15 Thr Lys Pro Thr Ile Gln Arg Tyr Lys Gly Leu Gly Glu Met Asp Asp  
 580 585 590  
 His Gln Leu Trp Glu Thr Thr Met Asp Pro Glu His Arg Leu Met Ala  
 595 600 605  
 Arg Val Ser Val Asp Asp Ala Ala Glu Ala Asp Lys Ile Phe Asp Met  
 610 615 620  
 25 Leu Met Gly Asp Arg Val Glu Pro Arg Arg Glu Phe Ile Glu Glu Asn  
 625 630 635 640  
 Ala Val Tyr Ser Thr Leu Asp Val  
 645  
 30  
 <210> 174  
 <211> 88  
 <212> PRT  
 35 <213> Streptococcus pneumoniae  
 <400> 174  
 Met Gly Phe Thr Glu Glu Thr Val Arg Phe Lys Leu Asp Asp Ser Asn  
 1 5 10 15  
 40 Lys Lys Glu Ile Ser Glu Thr Leu Thr Asp Val Tyr Ala Ser Leu Asn  
 20 25 30  
 Asp Lys Gly Tyr Asn Pro Ile Asn Gln Ile Val Gly Tyr Val Leu Ser  
 35 40 45  
 Gly Asp Pro Ala Tyr Val Pro Arg Tyr Asn Asn Ala Arg Asn Gln Ile  
 50 55 60  
 50 Arg Lys Tyr Glu Arg Asp Glu Ile Val Glu Glu Leu Val Arg Tyr Tyr  
 65 70 75 80  
 Leu Lys Gly Gln Gly Val Asp Leu  
 85  
 55  
 <210> 175

<211> 198  
 <212> PRT  
 <213> Streptococcus pneumoniae

- 5 <400> 175  
 Met Val Asn Tyr Pro His Lys Val Ser Ser Gln Asp Arg Gln Thr Ser  
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- 10 Leu Ser Gln Pro Lys Asn Phe Ala Asn Arg Gly Met Ser Phe Glu Lys  
                     20                    25                    30
- Met Ile Asn Ala Thr Asn Asp Tyr Tyr Leu Ser Gln Gly Leu Ala Val  
             35                    40                    45
- 15 Ile His Lys Lys Pro Thr Pro Ile Gln Ile Val Gln Val Asp Tyr Pro  
             50                    55                    60
- Gln Arg Ser Arg Ala Lys Ile Val Glu Ala Tyr Phe Arg Gln Ala Ser  
     65                    70                    75                    80
- 20 Thr Thr Asp Tyr Ser Gly Val Tyr Asn Gly Tyr Tyr Ile Asp Phe Glu  
                     85                    90                    95
- 25 Val Lys Glu Thr Lys Gln Lys Arg Ala Ile Pro Met Lys Asn Phe His  
                     100                    105                    110
- Pro His Gln Ile Gln His Met Glu Gln Val Leu Ala Gln Gln Gly Ile  
             115                    120                    125
- 30 Cys Phe Val Leu Leu His Phe Ser Ser Gln Gln Glu Thr Tyr Leu Leu  
             130                    135                    140
- Pro Ala Phe Asp Leu Ile Arg Phe Tyr His Gln Asp Lys Gly Gln Lys  
     145                    150                    155                    160
- 35 Ser Met Pro Leu Glu Tyr Ile Arg Glu Tyr Gly Tyr Glu Ile Lys Ala  
                     165                    170                    175
- 40 Gly Ala Phe Pro Gln Ile Pro Tyr Leu Asn Val Ile Lys Glu His Leu  
                     180                    185                    190
- Leu Gly Gly Lys Thr Arg  
     195
- 45 <210> 176  
 <211> 288  
 <212> PRT  
 <213> Streptococcus pneumoniae
- 50 <400> 176  
 Met Ala Leu Phe Ser Lys Lys Asp Lys Tyr Ile Arg Ile Asn Pro Asn  
     1                    5                    10                    15
- 55 Arg Ser Val Arg Glu Lys Pro Gln Ala Lys Pro Glu Val Pro Asp Glu  
             20                    25                    30

Leu Phe Ser Gln Cys Pro Gly Cys Lys His Thr Ile Tyr Gln Lys Asp  
           35                          40                          45  
 5 Leu Gly Ser Glu Arg Ile Cys Pro His Cys Ser Tyr Thr Phe Arg Ile  
       50                          55                          60  
 Ser Ala Gln Glu Arg Leu Ala Leu Thr Ile Asp Met Gly Thr Phe Lys  
       65                          70                          75                          80  
 10 Glu Leu Phe Thr Gly Ile Glu Ser Lys Asp Pro Leu His Phe Pro Gly  
                           85                          90                          95  
 Tyr Gln Lys Lys Leu Ala Ser Met Arg Glu Lys Thr Gly Leu His Glu  
                           100                          105                          110  
 15 Ala Val Val Thr Gly Thr Ala Leu Ile Lys Gly Gln Thr Val Ala Leu  
                           115                          120                          125  
 Gly Ile Met Asp Ser Asn Phe Ile Met Ala Ser Met Gly Thr Val Val  
       130                          135                          140  
 Gly Glu Lys Ile Thr Arg Leu Phe Glu Tyr Ala Thr Val Glu Lys Leu  
       145                          150                          155                          160  
 25 Pro Val Val Leu Phe Thr Ala Ser Gly Gly Ala Arg Met Gln Glu Gly  
                           165                          170                          175  
 Ile Met Ser Leu Met Gln Met Ala Lys Ile Ser Ala Ala Val Lys Arg  
                           180                          185                          190  
 30 His Ser Asn Ala Gly Leu Phe Tyr Leu Thr Ile Leu Thr Asp Pro Thr  
                           195                          200                          205  
 Thr Gly Gly Val Thr Ala Ser Phe Ala Met Glu Gly Asp Ile Ile Leu  
       210                          215                          220  
 Ala Glu Pro Gln Ser Leu Val Gly Phe Ala Gly Arg Arg Val Ile Glu  
       225                          230                          235                          240  
 40 Asn Thr Val Arg Glu Ser Leu Pro Glu Asp Phe Gln Lys Ala Glu Phe  
                           245                          250                          255  
 Leu Leu Glu His Gly Phe Val Asp Ala Ile Val Lys Arg Arg Asp Leu  
                           260                          265                          270  
 45 Pro Asp Thr Ile Ala Ser Leu Val Arg Leu His Gly Gly Ser Pro Arg  
                           275                          280                          285  
 50  
 <210> 177  
 <211> 139  
 55 <212> PRT  
 <213> Streptococcus pneumoniae

<400> 177  
 Met Arg Ile Met Gly Leu Asp Val Gly Ser Lys Thr Val Gly Val Ala  
 1 5 10 15  
 5 Ile Ser Asp Pro Leu Gly Phe Thr Ala Gln Gly Leu Glu Ile Ile Gln  
 20 25 30  
 Ile Asn Glu Glu Gln Gly Gln Phe Gly Ser Asp Arg Val Lys Glu Leu  
 35 40 45  
 10 Val Asp Thr Tyr Lys Val Glu Arg Phe Val Val Gly Leu Pro Lys Asn  
 50 55 60  
 15 Met Asn Asn Thr Ser Gly Pro Arg Val Glu Ala Ser Gln Ala Tyr Gly  
 65 70 75 80  
 Ala Lys Leu Glu Glu Phe Phe Gly Leu Pro Val Asp Tyr Gln Asp Glu  
 85 90 95  
 20 Arg Leu Thr Thr Val Ala Ala Glu Arg Met Leu Ile Glu Gln Ala Asp  
 100 105 110  
 Ile Ser Arg Asn Lys Arg Lys Lys Val Ile Asp Lys Leu Ala Ala Gln  
 115 120 125  
 25 Leu Ile Leu Gln Asn Tyr Leu Asp Arg Lys Phe  
 130 135  
 30 <210> 178  
 <211> 398  
 <212> PRT  
 <213> Streptococcus pneumoniae  
 35 <400> 178  
 Met Ala Lys Leu Thr Val Lys Asp Val Asp Leu Lys Gly Lys Lys Val  
 1 5 10 15  
 40 Leu Val Arg Val Asp Phe Asn Val Pro Leu Lys Asp Gly Val Ile Thr  
 20 25 30  
 Asn Asp Asn Arg Ile Thr Ala Ala Leu Pro Thr Ile Lys Tyr Ile Ile  
 35 40 45  
 45 Glu Gln Gly Gly Arg Ala Ile Leu Phe Ser His Leu Gly Arg Val Lys  
 50 55 60  
 Glu Glu Ala Asp Lys Ala Gly Lys Ser Leu Ala Pro Val Ala Ala Asp  
 65 70 75 80  
 50 Leu Ala Ala Lys Leu Gly Gln Asp Val Val Phe Pro Gly Val Thr Arg  
 85 90 95  
 55 Gly Ala Glu Leu Glu Ala Ala Ile Asn Ala Leu Glu Asp Gly Gln Val  
 100 105 110  
 Leu Leu Val Glu Asn Thr Arg Tyr Glu Asp Val Asp Gly Lys Lys Glu

	115	120	125
5	Ser Lys Asn Asp Pro Glu Leu Gly Lys Tyr Trp Ala Ser Leu Gly Asp 130 135 140		
	Gly Ile Phe Val Asn Asp Ala Phe Gly Thr Ala His Arg Ala His Ala 145 150 155 160		
10	Ser Asn Val Gly Ile Ser Ala Asn Val Glu Lys Ala Val Ala Gly Phe 165 170 175		
	Leu Leu Glu Asn Glu Ile Ala Tyr Ile Gln Glu Ala Val Glu Thr Pro 180 185 190		
15	Glu Arg Pro Phe Val Ala Ile Leu Gly Gly Ser Lys Val Ser Asp Lys 195 200 205		
	Ile Gly Val Ile Glu Asn Leu Leu Glu Lys Ala Asp Lys Val Leu Ile 210 215 220		
20	Gly Gly Gly Met Thr Tyr Thr Phe Tyr Lys Ala Gln Gly Ile Glu Ile 225 230 235 240		
	Gly Asn Ser Leu Val Glu Glu Asp Lys Leu Asp Val Ala Lys Ala Leu 245 250 255		
25	Leu Glu Lys Ala Asn Gly Lys Leu Ile Leu Pro Val Asp Ser Lys Glu 260 265 270		
30	Ala Asn Ala Phe Ala Gly Tyr Thr Glu Val Arg Asp Thr Glu Gly Glu 275 280 285		
	Ala Val Ser Glu Gly Phe Leu Gly Leu Asp Ile Gly Pro Lys Ser Ile 290 295 300		
35	Ala Lys Phe Asp Glu Ala Leu Thr Gly Ala Lys Thr Val Val Trp Asn 305 310 315 320		
	Gly Pro Met Gly Val Phe Glu Asn Pro Asp Phe Gln Ala Gly Thr Ile 325 330 335		
40	Gly Val Met Asp Ala Ile Val Lys Gln Pro Gly Val Lys Ser Ile Ile 340 345 350		
45	Gly Gly Gly Asp Ser Ala Ala Ala Ile Asn Leu Gly Arg Ala Asp 355 360 365		
	Lys Phe Ser Trp Ile Ser Thr Gly Gly Gly Ala Ser Met Glu Leu Leu 370 375 380		
50	Glu Gly Lys Val Leu Pro Gln Leu Ala Ala Leu Thr Glu Lys 385 390 395		
55	<210> 179 <211> 165 <212> PRT		

&lt;213&gt; Streptococcus pneumoniae

&lt;400&gt; 179

5 Met Leu Lys Ser Glu Lys Gln Ser Arg Tyr Gln Met Leu Asn Glu Glu  
 1 5 10 15  
 Leu Ser Phe Leu Leu Glu Gly Glu Thr Asn Val Leu Ala Asn Leu Ser  
 20 25 30  
 10 Asn Ala Ser Ala Leu Ile Lys Ser Arg Phe Pro Asn Thr Val Phe Ala  
 35 40 45  
 Gly Phe Tyr Leu Phe Asp Gly Lys Glu Leu Val Leu Gly Pro Phe Gln  
 50 55 60  
 15 Gly Gly Val Ser Cys Ile Arg Ile Ala Leu Gly Lys Gly Val Cys Gly  
 65 70 75 80  
 Glu Ala Ala His Phe Gln Glu Thr Val Ile Val Gly Asp Val Thr Thr  
 85 90 95  
 Tyr Leu Asn Tyr Ile Ser Cys Asp Ser Leu Ala Lys Ser Glu Ile Val  
 100 105 110  
 25 Val Pro Met Met Lys Asn Gly Gln Leu Leu Gly Val Leu Asp Leu Asp  
 115 120 125  
 Ser Ser Glu Ile Glu Asp Tyr Asp Ala Met Asp Arg Asp Tyr Leu Glu  
 130 135 140  
 30 Gln Phe Val Ala Ile Leu Leu Glu Lys Thr Ala Trp Asp Phe Thr Met  
 145 150 155 160  
 35 Phe Glu Glu Lys Ser  
 165

&lt;210&gt; 180

&lt;211&gt; 209

40 &lt;212&gt; PRT

&lt;213&gt; Streptococcus pneumoniae

&lt;400&gt; 180

45 Met Thr Ile Glu Leu Leu Thr Pro Phe Thr Lys Val Glu Leu Glu Pro  
 1 5 10 15  
 Glu Ile Lys Glu Lys Lys Arg Lys Gln Val Gly Ile Leu Gly Gly Asn  
 20 25 30  
 50 Phe Asn Pro Val His Asn Ala His Leu Ile Val Ala Asp Gln Val Arg  
 35 40 45  
 Gln Gln Leu Gly Leu Asp Gln Val Leu Leu Met Pro Glu Tyr Gln Pro  
 50 55 60  
 55 Pro His Val Asp Lys Lys Glu Thr Ile Pro Glu His His Arg Leu Lys  
 65 70 75 80

Met Leu Glu Leu Ala Ile Glu Gly Ile Asp Gly Leu Val Ile Glu Thr  
85 90 95

5 Ile Glu Leu Glu Arg Lys Gly Ile Ser Tyr Thr Tyr Asp Thr Met Lys  
100 105 110

Ile Leu Thr Glu Lys Asn Pro Asp Thr Asp Tyr Tyr Phe Ile Ile Gly  
115 120 125

10 Ala Asp Met Val Asp Tyr Leu Pro Lys Trp Tyr Arg Ile Asp Glu Leu  
130 135 140

Val Asp Met Val Gln Phe Val Gly Val Gln Arg Pro Arg Tyr Lys Val  
15 145 150 155 160

Gly Thr Ser Tyr Pro Val Ile Trp Val Asp Val Pro Leu Met Asp Ile  
165 170 175

20 Ser Ser Ser Met Val Arg Ala Phe Leu Ala Gln Gly Arg Lys Pro Asn  
180 185 190

Phe Leu Leu Pro Gln Pro Val Leu Asp Tyr Ile Glu Lys Glu Gly Leu  
25 195 200 205

Tyr

30 <210> 181  
<211> 255  
<212> PRT  
<213> Streptococcus pneumoniae

35 <400> 181  
Met Asn Ile Ala Lys Ile Val Arg Glu Ala Arg Glu Gln Ser Arg Leu  
1 5 10 15

40 Thr Thr Leu Asp Phe Ala Thr Gly Ile Phe Asp Glu Phe Ile Gln Leu  
20 25 30

His Gly Asp Arg Ser Phe Arg Asp Asp Gly Ala Val Val Gly Gly Ile  
35 40 45

45 Gly Trp Leu Gly Asp Gln Ala Val Thr Val Val Gly Ile Gln Lys Gly  
50 55 60

Lys Ser Leu Gln Asp Asn Leu Lys Arg Asn Phe Gly Gln Pro His Pro  
65 70 75 80

50 Glu Gly Tyr Arg Lys Ala Leu Arg Leu Met Lys Gln Ala Glu Lys Phe  
85 90 95

Gly Arg Pro Val Val Thr Phe Ile Asn Thr Ala Gly Ala Tyr Pro Gly  
55 100 105 110

Val Gly Ala Glu Glu Arg Gly Gln Gly Glu Ala Ile Ala Arg Asn Leu

115                      120                      125  
 Met Glu Met Ser Asp Leu Lys Val Pro Ile Ile Ala Ile Ile Ile Gly  
 130                      135                      140  
 5    Glu Gly Gly Ser Gly Gly Ala Leu Ala Leu Ala Val Ala Asp Arg Val  
 145                      150                      155                      160  
 10    Trp Met Leu Glu Asn Ser Ile Tyr Ala Ile Leu Ser Pro Glu Gly Phe  
 165                      170                      175  
 Ala Ser Ile Leu Trp Lys Asp Gly Thr Arg Ala Met Glu Ala Ala Glu  
 180                      185                      190  
 15    Leu Met Lys Ile Thr Ser His Glu Leu Leu Glu Met Asp Val Val Asp  
 195                      200                      205  
 Lys Val Ile Ser Glu Val Gly Leu Ser Ser Lys Glu Leu Ile Lys Ser  
 210                      215                      220  
 20    Val Lys Lys Glu Leu Gln Thr Glu Leu Ala Arg Leu Ser Gln Lys Pro  
 225                      230                      235                      240  
 25    Leu Glu Glu Leu Leu Glu Glu Arg Tyr Gln Arg Phe Arg Lys Tyr  
 245                      250                      255  
 30    <210> 182  
 <211> 169  
 <212> PRT  
 <213> Streptococcus pneumoniae  
 <400> 182  
 35    Met Ile Ile Lys Val Glu Met Ala Asp Val Glu Val Leu Ala Lys Ile  
 1                      5                      10                      15  
 Ala Lys Gln Thr Phe Arg Glu Thr Phe Ala Tyr Asp Asn Thr Glu Glu  
 20                      25                      30  
 40    Gln Leu Gln Glu Tyr Phe Glu Glu Ala Tyr Ser Leu Lys Thr Leu Ser  
 35                      40                      45  
 Thr Glu Leu Gly Asn Pro Asp Ser Glu Thr Tyr Phe Ile Met His Glu  
 50                      55                      60  
 45    Glu Glu Ile Ala Gly Phe Leu Lys Val Asn Trp Gly Ser Ala Gln Thr  
 65                      70                      75                      80  
 50    Glu Arg Glu Leu Glu Asp Ala Phe Glu Ile Gln Arg Leu Tyr Val Leu  
 85                      90                      95  
 Gln Lys Phe Gln Gly Phe Gly Leu Gly Lys Gln Leu Phe Glu Phe Ala  
 100                      105                      110  
 55    Leu Glu Leu Ala Thr Lys Asn Ser Phe Ser Trp Ala Trp Leu Gly Val  
 115                      120                      125



Trp Glu His Asn Thr Lys Ala Gln Ala Phe Tyr Asn Arg Tyr Gly Phe  
 130 135 140  
 5 Glu Lys Phe Ser Gln His His Phe Met Val Gly Gln Lys Val Asp Thr  
 145 150 155 160  
 Asp Trp Leu Leu Arg Lys Lys Leu Arg  
 165  
 10 <210> 183  
 <211> 529  
 <212> PRT  
 <213> Streptococcus pneumoniae  
 15 <400> 183  
 Met Leu Arg Gly Thr Ala Leu Leu Thr Ala Ser Asn Phe Ile Ser Arg  
 1 5 10 15  
 20 Leu Leu Gly Ala Val Tyr Ile Ile Pro Trp Tyr Ile Trp Met Gly Ala  
 20 25 30  
 Tyr Ala Ala Lys Ala Asn Gly Leu Phe Thr Met Gly Tyr Thr Ile Tyr  
 35 40 45  
 25 Ala Trp Phe Leu Leu Val Ser Thr Ala Gly Ile Pro Val Ala Val Ala  
 50 55 60  
 30 Lys Gln Val Ala Lys Tyr Asn Thr Met Arg Glu Glu Glu His Ser Phe  
 65 70 75 80  
 Ala Leu Ile Arg Ser Phe Leu Gly Phe Met Thr Gly Leu Gly Leu Val  
 85 90 95  
 35 Phe Ala Leu Val Leu Tyr Val Phe Ala Pro Trp Leu Ala Asp Leu Ser  
 100 105 110  
 Gly Val Gly Lys Asp Leu Ile Pro Ile Met Gln Ser Leu Ala Trp Gly  
 115 120 125  
 40 Val Leu Ile Phe Pro Ser Met Ser Val Ile Arg Gly Phe Phe Gln Gly  
 130 135 140  
 45 Met Asn Asn Leu Lys Pro Tyr Ala Met Ser Gln Ile Ala Glu Gln Val  
 145 150 155 160  
 Ile Arg Val Ile Trp Met Leu Leu Ala Thr Phe Ile Ile Met Lys Leu  
 165 170 175  
 50 Gly Ser Gly Asp Tyr Leu Ala Ala Val Thr Gln Ser Thr Phe Ala Ala  
 180 185 190  
 Phe Val Gly Met Val Ala Ser Phe Ala Val Leu Ile Tyr Phe Leu Ala  
 195 200 205  
 55 Gln Glu Ser Ser Leu Lys Arg Val Phe Glu Thr Gly Asp Lys Ile Asn  
 210 215 220

Ser Lys Arg Leu Leu Val Asp Thr Ile Lys Glu Ala Ile Pro Phe Ile  
 225 230 235 240  
 5 Leu Thr Gly Ser Ala Ile Gln Ile Phe Gln Ile Leu Asp Gln Leu Thr  
 245 250 255  
 Phe Ile Asn Ser Met Ser Trp Phe Thr Asn Tyr Ser Asn Glu Asp Leu  
 260 265 270  
 10 Val Val Met Phe Ser Tyr Phe Ser Ala Asn Pro Asn Lys Ile Thr Met  
 275 280 285  
 Ile Leu Ile Ser Val Gly Val Ser Ile Gly Ser Val Gly Leu Pro Leu  
 15 290 295 300  
 Leu Thr Glu Asn Tyr Val Lys Gly Asp Leu Lys Ala Ala Ser Arg Leu  
 305 310 315 320  
 20 Val Gln Asp Ser Leu Thr Leu Leu Phe Met Phe Leu Leu Pro Ala Thr  
 325 330 335  
 Val Gly Val Val Met Val Gly Glu Pro Leu Tyr Thr Val Phe Tyr Gly  
 340 345 350  
 25 Lys Pro Asp Ser Leu Ala Leu Gly Leu Phe Val Phe Ala Val Leu Gln  
 355 360 365  
 Ser Ile Ile Leu Gly Leu Tyr Met Val Leu Ser Pro Met Leu Gln Ala  
 30 370 375 380  
 Met Phe Arg Asn Arg Lys Ala Val Leu Tyr Phe Ile Tyr Gly Ser Ile  
 385 390 395 400  
 35 Ala Lys Leu Val Leu Gln Leu Pro Thr Ile Ala Leu Phe His Ser Tyr  
 405 410 415  
 Gly Pro Leu Ile Ser Thr Thr Ile Ala Leu Ile Ile Pro Asn Val Leu  
 420 425 430  
 40 Met Tyr Arg Asp Ile Cys Lys Val Thr Gly Val Lys Arg Lys Val Ile  
 435 440 445  
 Leu Lys Arg Thr Ile Leu Ile Ser Leu Leu Thr Leu Val Met Phe Leu  
 45 450 455 460  
 Leu Ile Gly Thr Ile Gln Trp Leu Leu Gly Phe Phe Phe Gln Pro Ser  
 465 470 475 480  
 50 Gly Arg Leu Trp Ser Phe Phe Tyr Val Ala Leu Val Gly Ala Met Gly  
 485 490 495  
 Gly Gly Leu Tyr Met Val Met Ser Leu Arg Thr Tyr Leu Leu Asp Lys  
 500 505 510  
 55 Val Ile Gly Lys Ala Gln Ala Asp Arg Leu Arg Ala Lys Phe Lys Leu  
 515 520 525

Ser

5

&lt;210&gt; 184

&lt;211&gt; 155

&lt;212&gt; PRT

&lt;213&gt; Streptococcus pneumoniae

10

&lt;400&gt; 184

Met Ser Asp Lys Ile Gly Leu Phe Thr Gly Ser Phe Asp Pro Met Thr  
 1 5 10 15

15

Asn Gly His Leu Asp Ile Ile Glu Arg Ala Ser Arg Leu Phe Asp Lys  
 20 25 30

Leu Tyr Val Gly Ile Phe Phe Asn Pro His Lys Gln Gly Phe Leu Pro  
 35 40 45

20

Ile Glu Asn Arg Lys Arg Gly Leu Glu Lys Ala Leu Gly His Leu Glu  
 50 55 60

25

Asn Val Glu Val Val Ala Ser His Asp Glu Leu Val Val Asp Val Ala  
 65 70 75 80

Lys Arg Leu Gly Ala Thr Cys Leu Val Arg Gly Leu Arg Asn Ala Ser  
 85 90 95

30

Asp Leu Gln Tyr Glu Ala Ser Phe Asp Tyr Tyr Asn His Gln Leu Ser  
 100 105 110

Ser Asp Ile Glu Thr Ile Tyr Leu His Ser Arg Pro Glu His Leu Tyr  
 115 120 125

35

Ile Ser Ser Ser Gly Val Arg Glu Leu Leu Lys Phe Gly Gln Asp Ile  
 130 135 140

40

Ala Cys Tyr Val Pro Glu Ser Ile Trp Arg Lys  
 145 150 155

45

&lt;210&gt; 185

&lt;211&gt; 143

&lt;212&gt; PRT

&lt;213&gt; Streptococcus pneumoniae

&lt;400&gt; 185

Met Thr Ile Leu Phe Val Val Ile Ser Ala Ser Phe Leu Tyr Met Val  
 1 5 10 15

50

Ser Leu Ser Met Lys Pro Tyr Gln Thr Ala Lys Ser Glu Gly Glu Lys  
 20 25 30

55

Leu Ala Gln Gln Tyr Ala Gly Leu Glu Gln Ala Asp Gln Val Asp Leu  
 35 40 45

Tyr Asn Gly Leu Glu Ser Tyr Tyr Ser Val Leu Gly Arg Asn Lys Gln  
 50 55 60  
 5 Gln Glu Ala Leu Ala Val Leu Ile Gly Lys Asp Asp His Lys Ile Tyr  
 65 70 75 80  
 Val Tyr Gln Leu Asn Gln Gly Val Ser Gln Glu Lys Ala Glu Thr Val  
 85 90 95  
 10 Ser Lys Glu Lys Gly Ala Gly Glu Ile Asp Lys Ile Ile Phe Gly Arg  
 100 105 110  
 Tyr Gln Asp Lys Pro Ile Trp Glu Val Lys Ser Gly Ser Asp Phe Tyr  
 115 120 125  
 15 Leu Val Asp Phe Glu Thr Gly Ala Leu Val Asn Lys Glu Gly Leu  
 130 135 140  
 20 <210> 186  
 <211> 243  
 <212> PRT  
 <213> Streptococcus pneumoniae  
 25 <400> 186  
 Met Ile Asp Ile His Ser His Ile Val Phe Asp Val Asp Asp Gly Pro  
 1 5 10 15  
 30 Lys Ser Arg Glu Glu Ser Lys Ala Leu Leu Thr Glu Ala Tyr Arg Gln  
 20 25 30  
 Gly Val Arg Thr Ile Val Ser Thr Ser His Arg Arg Lys Gly Met Phe  
 35 40 45  
 35 Glu Thr Pro Glu Glu Lys Ile Ala Glu Asn Phe Leu Gln Val Arg Glu  
 50 55 60  
 Ile Ala Lys Glu Val Ala Ser Asp Leu Val Ile Ala Tyr Gly Ala Glu  
 65 70 75 80  
 40 Ile Tyr Tyr Thr Pro Asp Val Leu Asp Lys Leu Glu Asn Asn Arg Ile  
 85 90 95  
 45 Pro Thr Leu Asn Asn Ser Arg Tyr Ala Leu Ile Glu Phe Ser Met Asn  
 100 105 110  
 Thr Pro Tyr Arg Asp Ile His Ser Ala Leu Asn Lys Ile Leu Met Leu  
 115 120 125  
 50 Gly Ile Thr Pro Val Ile Ala His Ile Glu Arg Tyr Asp Val Leu Glu  
 130 135 140  
 Asn Asn Glu Lys Arg Val Arg Glu Leu Ile Asp Met Gly Cys Tyr Thr  
 145 150 155 160  
 55 Gln Ile Asn Ser Ser His Val Leu Lys Ser Lys Leu Phe Gly Glu Pro  
 165 170 175

Tyr Lys Phe Met Lys Lys Arg Ala Gln Tyr Phe Leu Glu Arg Asp Leu  
 180 185 190  
 5 Val His Ile Ile Ala Ser Asp Met His Asn Val Asp Gly Arg Pro Pro  
 195 200 205  
 His Met Ala Glu Ala Tyr Asp Leu Val Ser Gln Lys Tyr Gly Glu Ala  
 210 215 220  
 10 Lys Ala Gln Glu Leu Phe Ile Asp Asn Pro Arg Lys Ile Val Met Asp  
 225 230 235 240  
 Gln Leu Ile  
 15  
 <210> 187  
 <211> 308  
 20 <212> PRT  
 <213> Streptococcus pneumoniae  
 <400> 187  
 25 Met Ser Thr Ile Asp Lys Glu Lys Phe Gln Phe Val Lys Arg Asp Asp  
 1 5 10 15  
 Phe Ala Ser Glu Thr Ile Asp Ala Pro Ala Tyr Ser Tyr Trp Lys Ser  
 20 25 30  
 30 Val Phe Lys Gln Phe Met Lys Lys Lys Ser Thr Val Val Met Leu Gly  
 35 40 45  
 Ile Leu Val Ala Ile Ile Leu Ile Ser Phe Ile Tyr Pro Met Phe Ser  
 50 55 60  
 35 Lys Phe Asp Phe Asn Asp Val Ser Lys Val Asn Asp Phe Ser Val Arg  
 65 70 75 80  
 40 Tyr Ile Lys Pro Asn Ala Glu His Trp Phe Gly Thr Asp Ser Asn Gly  
 85 90 95  
 Lys Ser Leu Phe Asp Gly Val Trp Phe Gly Ala Arg Asn Ser Ile Leu  
 100 105 110  
 45 Ile Ser Val Ile Ala Thr Val Ile Asn Leu Val Ile Gly Val Phe Val  
 115 120 125  
 Gly Gly Ile Trp Gly Ile Ser Lys Ser Val Asp Arg Val Met Met Glu  
 130 135 140  
 50 Val Tyr Asn Val Ile Ser Asn Ile Pro Pro Leu Leu Ile Val Ile Val  
 145 150 155 160  
 55 Leu Thr Tyr Ser Ile Gly Ala Gly Phe Trp Asn Leu Ile Phe Ala Met  
 165 170 175  
 Ser Val Thr Thr Trp Ile Gly Ile Ala Phe Met Ile Arg Val Gln Ile

180 185 190  
 Leu Arg Tyr Arg Asp Leu Glu Tyr Asn Leu Ala Ser Arg Thr Leu Gly  
 195 200 205  
 5 Thr Pro Thr Leu Lys Ile Val Ala Lys Asn Ile Met Pro Gln Leu Val  
 210 215 220  
 10 Ser Val Ile Val Thr Thr Met Thr Gln Met Leu Pro Ser Phe Ile Ser  
 225 230 235 240  
 Tyr Glu Ala Phe Leu Ser Phe Phe Gly Leu Gly Leu Pro Ile Thr Val  
 245 250 255  
 15 Pro Ser Leu Gly Arg Leu Ile Ser Asp Tyr Ser Gln Asn Val Thr Thr  
 260 265 270  
 Asn Ala Tyr Leu Phe Trp Ile Pro Leu Thr Thr Leu Val Leu Val Ser  
 275 280 285  
 20 Leu Ser Leu Phe Val Val Gly Gln Asn Leu Ala Asp Ala Ser Asp Pro  
 290 295 300  
 25 Arg Thr His Arg  
 305  
 <210> 188  
 <211> 77  
 30 <212> PRT  
 <213> Streptococcus pneumoniae  
 <400> 188  
 35 Met Tyr Asn Leu Leu Leu Thr Ile Leu Leu Val Leu Ser Val Val Ile  
 1 5 10 15  
 Val Ile Ala Ile Phe Met Gln Pro Thr Lys Asn Gln Ser Ser Asn Val  
 20 25 30  
 40 Phe Asp Ala Ser Ser Gly Asp Leu Phe Glu Arg Ser Lys Ala Arg Gly  
 35 40 45  
 Phe Glu Ala Val Met Gln Arg Leu Thr Gly Ile Leu Val Phe Phe Trp  
 50 55 60  
 45 Leu Ala Ile Ala Leu Ala Leu Thr Val Leu Ser Ser Arg  
 65 70 75  
 50 <210> 189  
 <211> 369  
 <212> PRT  
 <213> Streptococcus pneumoniae  
 55 <400> 189  
 Met Phe Arg Arg Asn Lys Leu Phe Phe Trp Thr Thr Glu Ile Leu Leu  
 1 5 10 15

Leu Thr Ile Ile Phe Tyr Leu Trp Arg Gln Met Gly Ser Leu Ile Asn  
 20 25 30  
 5 Pro Phe Val Ser Val Leu Asn Thr Ile Met Ile Pro Phe Leu Leu Gly  
 35 40 45  
 Gly Phe Leu Tyr Tyr Leu Thr Asn Pro Ile Val Thr Phe Leu Asn Lys  
 50 55 60  
 10 Val Cys Lys Leu Asn Arg Leu Leu Gly Ile Leu Ile Thr Leu Cys Thr  
 65 70 75 80  
 15 Leu Val Trp Gly Met Val Ile Gly Val Val Tyr Leu Leu Pro Ile Leu  
 85 90 95  
 Ile Asn Gln Leu Ser Ser Leu Ile Ile Ser Ser Gln Thr Ile Tyr Ser  
 100 105 110  
 20 Arg Val Gln Asp Leu Ile Ile Asp Leu Ser Asn Tyr Pro Ala Leu Gln  
 115 120 125  
 Asn Leu Asp Val Glu Ala Thr Ile Gln Gln Leu Asn Leu Ser Tyr Val  
 130 135 140  
 25 Asp Ile Leu Gln Asn Ile Leu Asn Ser Val Ser Asn Ser Val Gly Ser  
 145 150 155 160  
 30 Val Leu Ser Ala Leu Ile Ser Thr Val Leu Ile Leu Ile Met Thr Pro  
 165 170 175  
 Val Phe Leu Val Tyr Phe Leu Leu Asp Gly His Lys Phe Leu Pro Met  
 180 185 190  
 35 Leu Glu Arg Thr Ile Leu Lys Arg Asp Arg Leu His Ile Ala Gly Leu  
 195 200 205  
 Leu Lys Asn Leu Asn Ala Thr Ile Ala Arg Tyr Ile Ser Gly Val Ser  
 210 215 220  
 40 Ile Asp Ala Ile Ile Ile Gly Cys Leu Ala Tyr Ile Gly Tyr Ser Ile  
 225 230 235 240  
 45 Ile Gly Leu Lys Tyr Ala Leu Val Phe Ala Ile Phe Ser Gly Val Ala  
 245 250 255  
 Asn Leu Ile Pro Tyr Val Gly Pro Ser Ile Gly Leu Ile Pro Met Ile  
 260 265 270  
 50 Ile Ala Asn Ile Phe Thr Val Pro His Arg Leu Leu Ile Ala Val Ile  
 275 280 285  
 Tyr Met Leu Val Val Gln Gln Val Asp Gly Asn Ile Leu Tyr Pro Arg  
 290 295 300  
 55 Ile Val Gly Ser Val Met Lys Val His Pro Ile Thr Ile Leu Val Leu  
 305 310 315 320

Leu Leu Leu Ser Ser Asn Ile Tyr Gly Val Val Gly Met Ile Val Ala  
 325 330 335  
 5 Val Pro Thr Tyr Ser Ile Leu Lys Glu Ile Ser Lys Phe Leu Ser Arg  
 340 345 350  
 Leu Tyr Glu Asn His Lys Ile Met Lys Glu Arg Glu Arg Glu Leu Ala  
 355 360 365  
 10 Lys  
 15 <210> 190  
 <211> 451  
 <212> PRT  
 <213> Streptococcus pneumoniae  
 20 <400> 190  
 Met Tyr Gln Ala Leu Tyr Arg Lys Tyr Arg Ser Gln Asn Phe Ser Gln  
 1 5 10 15  
 Leu Val Gly Gln Glu Val Val Ala Lys Thr Leu Lys Gln Ala Val Glu  
 25 20 25 30  
 Gln Glu Lys Ile Ser His Ala Tyr Leu Phe Ser Gly Pro Arg Gly Thr  
 35 40 45  
 30 Gly Lys Thr Ser Val Ala Lys Ile Phe Ala Lys Ala Met Asn Cys Pro  
 50 55 60  
 Asn Gln Val Gly Gly Glu Pro Cys Asn Asn Cys Tyr Ile Cys Gln Ala  
 65 70 75 80  
 35 Val Thr Asp Gly Ser Leu Glu Asp Val Ile Glu Met Asp Ala Ala Ser  
 85 90 95  
 40 Asn Asn Gly Val Asp Glu Ile Arg Glu Ile Arg Asp Lys Ser Thr Tyr  
 100 105 110  
 Ala Pro Ser Leu Ala Arg Tyr Lys Val Tyr Ile Ile Asp Glu Val His  
 115 120 125  
 45 Met Leu Ser Thr Gly Ala Phe Asn Ala Leu Leu Lys Thr Leu Glu Glu  
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 Pro Thr Gln Asn Val Val Phe Ile Leu Ala Thr Thr Glu Leu His Lys  
 145 150 155 160  
 50 Ile Pro Ala Thr Ile Leu Ser Arg Val Gln Arg Phe Glu Phe Lys Ser  
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 55 Ile Lys Thr Gln Asp Ile Lys Glu His Ile His Tyr Ile Leu Glu Lys  
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	195	200	205
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	Ser Leu Thr Gln Gly Asn Glu Leu Thr Thr Ala Ile Ser Glu Glu Ile 225 230 235 240		
10	Thr Gly Thr Ile Ser Leu Ser Ala Leu Asp Asp Tyr Val Ala Ala Leu 245 250 255		
	Ser Gln Gln Asp Val Pro Lys Ala Leu Ser Cys Leu Asn Leu Leu Phe 260 265 270		
15	Asp Asn Gly Lys Ser Met Thr Arg Phe Val Thr Asp Leu Leu His Tyr 275 280 285		
	Leu Arg Asp Leu Leu Ile Val Gln Thr Gly Gly Glu Asn Thr His His 290 295 300		
20	Ser Ser Val Phe Val Glu Asn Leu Ala Leu Pro Gln Lys Asn Leu Phe 305 310 315 320		
	Glu Met Ile Arg Leu Ala Thr Val Asn Leu Ala Asp Ile Lys Ser Ser 325 330 335		
25	Leu Gln Pro Lys Ile Tyr Ala Glu Met Met Thr Val Arg Leu Ala Glu 340 345 350		
	Ile Lys Pro Glu Pro Ala Leu Ser Gly Ala Val Glu Asn Glu Ile Ala 355 360 365		
30	Thr Leu Arg Gln Glu Val Ala Arg Leu Lys Gln Glu Leu Ser Asn Ala 370 375 380		
35	Gly Ala Val Pro Lys Gln Val Ala Pro Ala Pro Ser Arg Pro Ala Thr 385 390 395 400		
	Gly Lys Thr Val Tyr Arg Val Asp Arg Asn Lys Val Gln Ser Ile Leu 405 410 415		
40	Gln Glu Ala Val Glu Asn Pro Asp Leu Thr Arg Gln Asn Leu Ile Arg 420 425 430		
	Leu Gln Asn Ala Trp Gly Glu Val Ile Glu Ser Leu Gly Gly Pro Asp 435 440 445		
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	<211> 662		
	<212> PRT		
55	<213> Streptococcus pneumoniae		
	<400> 191		

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 20 25 30  
 Leu Thr Tyr Leu Phe Tyr Ser Leu Thr Phe Asn Pro Lys Ile Ala Glu  
 35 40 45  
 10 Ile Arg Gly Gly Thr Thr Ile Gln Ala Thr Leu Gly Phe Gly Met Phe  
 50 55 60  
 Val Val Thr Leu Ala Ser Ala Ile Ile Val Leu Tyr Ala Asn Ser Phe  
 65 70 75 80  
 15 Val Met Lys Lys Arg Ser Lys Glu Leu Gly Ile Tyr Gly Met Leu Gly  
 85 90 95  
 Leu Glu Lys Arg His Leu Ile Ser Met Thr Phe Lys Glu Leu Val Val  
 100 105 110  
 Phe Gly Ile Leu Thr Val Gly Ala Gly Ile Gly Ile Gly Ala Leu Phe  
 115 120 125  
 25 Asp Lys Leu Ile Phe Ala Phe Leu Leu Lys Leu Met Lys Leu Lys Val  
 130 135 140  
 Glu Leu Val Ala Thr Phe Gln Thr Lys Val Val Ile Thr Val Leu Val  
 145 150 155 160  
 30 Val Phe Gly Leu Ile Phe Leu Gly Leu Met Phe Leu Asn Ala Leu Arg  
 165 170 175  
 Ile Ala Arg Met Asn Ala Leu Gln Leu Ser Arg Glu Lys Ala Ser Gly  
 180 185 190  
 Glu Lys Lys Gly Arg Phe Leu Pro Leu Gln Thr Ile Leu Gly Ser Ile  
 195 200 205  
 40 Ser Leu Gly Ile Gly Tyr Tyr Leu Ala Leu Thr Val Lys Asp Pro Leu  
 210 215 220  
 Thr Ala Leu Thr Thr Phe Phe Ile Ala Val Leu Leu Val Ile Phe Gly  
 225 230 235 240  
 45 Thr Tyr Leu Leu Phe Asn Ala Gly Ile Thr Val Phe Leu Gln Ile Leu  
 245 250 255  
 Lys Lys Asn Lys Lys Tyr Tyr Tyr Gln Pro Asn Asn Leu Ile Ser Val  
 260 265 270  
 50 Ser Asn Leu Ile Phe Arg Met Lys Lys Asn Ala Val Gly Leu Ala Thr  
 275 280 285  
 55 Ile Ala Ile Leu Ser Thr Met Val Leu Val Thr Met Ser Ala Ala Thr  
 290 295 300

Ser Ile Phe Asn Ser Ala Glu Ser Phe Lys Lys Val Leu Asn Pro His  
 305 310 315 320  
 5 Asp Phe Gly Val Ser Gly Gln Asn Val Glu Lys Glu Asp Leu Asp Lys  
 325 330 335  
 Leu Leu Ser Gln Phe Ala Ser Asp Asn Gly Tyr Lys Ile Lys Glu Lys  
 340 345 350  
 10 Glu Val Phe Arg Tyr Thr Tyr Phe Gly Val Ala Asn Gln Glu Gly Asn  
 355 360 365  
 Lys Leu Thr Phe Phe Glu Lys Gly Gln Asn Arg Val Gln Pro Thr Thr  
 370 375 380  
 15 Val Phe Met Val Phe Asp Gln Lys Asp Tyr Glu Asn Met Thr Gly Gln  
 385 390 395 400  
 Lys Leu Ser Leu Ser Gly Asn Glu Val Gly Leu Phe Ala Lys Asn Asp  
 405 410 415  
 Gly Leu Lys Gly Gln Lys Thr Leu Ile Leu Asn Asp His Gln Phe Ser  
 420 425 430  
 25 Val Lys Glu Glu Phe Asn Lys Asp Phe Ile Val Asn His Val Pro Asn  
 435 440 445  
 Gln Phe Asn Ile Leu Thr Ala Asp Tyr Asn Tyr Leu Val Val Pro Asp  
 450 455 460  
 30 Leu Gln Ala Phe Leu Asn Gln Phe Pro Asp Ser Asp Ile Tyr Asn Gln  
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 Phe Tyr Gly Gly Met Asn Val Asn Val Ser Glu Glu Glu Gln Leu Lys  
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 Val Ala Glu Glu Tyr Glu Asn Tyr Leu Asn Gln Phe Asn Ala Gln Leu  
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 40 Asp Thr Glu Gly Ser Tyr Val Tyr Gly Ser Asn Leu Ala Asp Ala Ser  
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 Ser Gln Met Ser Ala Leu Phe Gly Gly Val Phe Phe Ile Gly Ile Phe  
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 45 Leu Ser Ile Ile Phe Met Val Gly Thr Val Leu Val Ile Tyr Tyr Lys  
 545 550 555 560  
 Gln Ile Ser Glu Gly Tyr Glu Asp Arg Glu Arg Phe Ile Ile Leu Gln  
 565 570 575  
 50 Lys Val Gly Leu Asp Gln Lys Gln Ile Lys Gln Thr Ile His Lys Gln  
 580 585 590  
 55 Val Leu Thr Val Phe Phe Leu Pro Leu Leu Phe Ala Phe Ile His Leu  
 595 600 605

Ala Phe Ala Tyr His Met Leu Ser Leu Ile Leu Lys Val Ile Gly Val  
 610 615 620  
 5 Leu Asp Thr Thr Met Met Leu Ile Val Thr Leu Ser Ile Cys Ala Ile  
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 Phe Leu Ile Ala Tyr Val Leu Ile Phe Met Ile Thr Ser Arg Ser Tyr  
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 <213> Streptococcus pneumoniae  
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 20 25 30  
 25 Ser Gly Phe Phe Gly Ser Leu Glu Met Ala Gln Phe Leu Ala Lys Ser  
 35 40 45  
 30 Leu Phe Cys Thr Asp Lys Val Gly Val Leu Pro Cys Glu Lys Cys Arg  
 50 55 60  
 Ser Cys Lys Leu Ile Glu Gln Glu Glu Phe Pro Asp Val Thr Leu Ile  
 65 70 75 80  
 35 Lys Pro Val Asn Gln Val Ile Lys Thr Glu Arg Ile Arg Glu Leu Val  
 85 90 95  
 40 Gly Gln Phe Ser Gln Ala Gly Ile Glu Ser Gln Gln Gln Val Phe Ile  
 100 105 110  
 Ile Glu Gln Ala Asp Lys Met His Pro Asn Ala Ala Asn Ser Leu Leu  
 115 120 125  
 45 Lys Val Ile Glu Glu Pro Gln Ser Glu Val Tyr Ile Phe Phe Leu Thr  
 130 135 140  
 Ser Asp Glu Glu Lys Met Leu Pro Thr Ile Arg Ser Arg Thr Gln Ile  
 145 150 155 160  
 50 Phe His Phe Lys Lys Gln Glu Glu Lys Leu Ile Leu Leu Leu Glu Gln  
 165 170 175  
 Met Gly Leu Val Lys Lys Lys Ala Thr Leu Leu Ala Lys Phe Ser Gln  
 180 185 190  
 55 Ser Arg Ala Glu Ala Glu Lys Leu Ala Asn Gln Ala Ser Phe Trp Thr  
 195 200 205

Leu Val Asp Glu Ser Glu Arg Leu Leu Thr Trp Leu Val Ala Lys Lys  
 210 215 220  
 5 Lys Glu Ser Tyr Leu Gln Val Ala Lys Leu Ala Asn Leu Ala Asp Asp  
 225 230 235 240  
 Lys Glu Lys Gln Asp Gln Val Leu Arg Ile Leu Glu Val Leu Cys Gly  
 245 250 255  
 10 Gln Asp Leu Leu Gln Val Arg Val Arg Val Ile Leu Gln Asp Leu Leu  
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 Glu Tyr Leu Val Leu Lys Glu Ile  
 290 295  
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 <212> PRT  
 <213> Streptococcus pneumoniae  
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 <400> 193  
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 20 25 30  
 Arg Val Glu Gly His Ser Met Asp Pro Thr Leu Ala Asp Gly Glu Ile  
 35 35 40 45  
 Leu Phe Val Val Lys His Leu Pro Ile Asp Arg Phe Asp Ile Val Val  
 50 55 60  
 40 Ala His Glu Glu Asp Gly Asn Lys Asp Ile Val Lys Arg Val Ile Gly  
 65 70 75 80  
 Met Pro Gly Asp Thr Ile Arg Tyr Glu Asn Asp Lys Leu Tyr Ile Asn  
 85 90 95  
 45 Asp Lys Glu Thr Asp Glu Pro Tyr Leu Ala Asp Tyr Ile Lys Arg Phe  
 100 105 110  
 Lys Asp Asp Lys Leu Gln Ser Thr Tyr Ser Gly Lys Gly Phe Glu Gly  
 115 120 125  
 50 Asn Lys Gly Thr Phe Phe Arg Ser Ile Ala Gln Lys Ala Gln Ala Phe  
 130 135 140  
 55 Thr Val Asp Val Asn Tyr Asn Thr Asn Phe Ser Phe Thr Val Pro Glu  
 145 150 155 160  
 Gly Glu Tyr Leu Leu Leu Gly Asp Asp Arg Leu Val Ser Ser Asp Ser

165 170 175  
 Arg His Val Gly Thr Phe Lys Ala Lys Asp Ile Thr Gly Glu Ala Lys  
 180 185 190  
 5 Phe Arg Phe Trp Pro Ile Thr Arg Ile Gly Thr Phe  
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 10 <210> 194  
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 <213> Streptococcus pneumoniae  
 15 <400> 194  
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 Ser Arg Glu Lys Lys Gly Phe Leu Gly Leu Phe Gly Lys Lys Pro Ala  
 35 40 45  
 25 Gln Val Asp Ile Glu Ala Ile Ser Glu Thr Thr Val Val Lys Ala Asn  
 50 55 60  
 Gln Gln Val Val Lys Gly Val Pro Lys Lys Ile Asn Asp Leu Asn Glu  
 65 70 75 80  
 30 Pro Val Lys Thr Val Ser Glu Glu Thr Val Asp Leu Gly His Val Val  
 85 90 95  
 35 Asn Ala Ile Lys Lys Ile Glu Glu Glu Gly Gln Gly Ile Ser Asp Glu  
 100 105 110  
 Val Lys Ala Glu Ile Leu Lys His Glu Arg His Ala Ser Thr Ile Leu  
 115 120 125  
 40 Glu Glu Thr Gly His Ile Glu Ile Leu Asn Glu Leu Gln Ile Glu Glu  
 130 135 140  
 Ala Met Arg Glu Glu Ala Gly Ala Asp Asp Leu Glu Thr Glu Gln Asp  
 145 150 155 160  
 45 Gln Thr Glu Asn Gln Asp Leu Lys Glu Met Gly Leu Lys Val Glu Gln  
 165 170 175  
 50 Ser Tyr Asp Ile Ala Gln Val Ala Thr Asp Val Thr Ala Tyr Val Gln  
 180 185 190  
 Ala Ile Val Asp Asp Met Asp Val Glu Ala Thr Leu Ser Asn Asp Tyr  
 195 200 205  
 55 Asn Arg Arg Ser Ile Asn Leu Gln Ile Asp Thr Asn Glu Pro Gly Arg  
 210 215 220

Ile Ile Gly Tyr His Gly Lys Val Leu Lys Ala Leu Gln Leu Leu Ala  
 225 230 235 240  
 5 Gln Asn Tyr Leu Tyr Asn Arg Tyr Ser Lys Thr Phe Tyr Val Thr Ile  
 245 250 255  
 Asn Val Asn Asp Tyr Val Glu His Arg Ala Glu Val Leu Gln Thr Tyr  
 260 265 270  
 10 Ala Gln Lys Leu Ala Asn Arg Val Leu Glu Glu Gly Arg Ser His Lys  
 275 280 285  
 Thr Asp Pro Met Ser Asn Ser Glu Arg Lys Ile Ile His Arg Ile Ile  
 290 295 300  
 15 Ser Arg Met Asp Gly Val Thr Ser Tyr Ser Glu Gly Asp Glu Pro Asn  
 305 310 315 320  
 20 Arg Tyr Val Val Val Asp Thr Glu  
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 <211> 460  
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 <213> Streptococcus pneumoniae  
 <400> 195  
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 35 Leu Glu His Val Phe Arg Ser Val Gly Ala Ile Gln Pro Glu Lys Thr  
 35 40 45  
 Val Thr Val Val Gly His Lys Ala Glu Leu Val Glu Glu Val Leu Ala  
 50 55 60  
 40 Gly Gln Thr Glu Phe Val Thr Gln Ser Glu Gln Leu Gly Thr Gly His  
 65 70 75 80  
 45 Ala Val Met Met Thr Glu Pro Ile Leu Glu Gly Val Ser Gly His Thr  
 85 90 95  
 Leu Val Ile Ala Gly Asp Thr Pro Leu Ile Thr Gly Glu Ser Leu Lys  
 100 105 110  
 50 Asn Leu Ile Asp Phe His Ile Asn His Lys Asn Val Ala Thr Ile Leu  
 115 120 125  
 Thr Ala Glu Thr Asp Asn Pro Phe Gly Tyr Gly Arg Ile Val Arg Asn  
 130 135 140  
 55 Asp Asn Ala Glu Val Leu Arg Ser Leu Leu Ser Arg Arg Met Leu Gln  
 145 150 155 160

Ile Leu Lys Ser Lys Ser Arg Lys Ser Thr Leu Val Thr Tyr Val Phe  
 165 170 175  
 5 Asp Asn Glu Arg Leu Phe Glu Ala Leu Lys Asn Ile Asn Thr Asn Asn  
 180 185 190  
 Ala Gln Gly Glu Tyr Tyr Ile Thr Asp Val Ile Gly Ile Phe Arg Glu  
 195 200 205  
 10 Thr Gly Glu Lys Val Gly Ala Tyr Thr Leu Lys Asp Phe Asp Glu Ser  
 210 215 220  
 Leu Gly Val Asn Asp Arg Val Ala Leu Ala Thr Ala Glu Ser Val Met  
 15 225 230 235 240  
 Arg Arg Arg Ile Asn His Lys His Met Val Asn Gly Val Ser Phe Val  
 245 250 255  
 20 Asn Pro Glu Ala Thr Tyr Ile Asp Ile Asp Val Glu Ile Ala Pro Glu  
 260 265 270  
 Val Gln Ile Glu Ala Asn Val Ile Leu Lys Gly Gln Thr Lys Ile Gly  
 275 280 285  
 25 Ala Glu Thr Val Leu Thr Asn Gly Thr Tyr Val Val Asp Ser Thr Ile  
 290 295 300  
 Gly Ala Gly Ala Val Ile Thr Asn Ser Met Ile Glu Glu Ser Ser Val  
 30 305 310 315 320  
 Ala Asp Gly Val Thr Val Gly Pro Tyr Ala His Ile Arg Pro Asn Ser  
 325 330 335  
 35 Ser Leu Gly Ala Gln Val His Ile Gly Asn Phe Val Glu Val Lys Gly  
 340 345 350  
 Ser Ser Ile Gly Glu Asn Thr Lys Ala Gly His Leu Thr Tyr Ile Gly  
 355 360 365  
 40 Asn Cys Glu Val Gly Ser Asn Val Asn Phe Gly Ala Gly Thr Ile Thr  
 370 375 380  
 Val Asn Tyr Asp Gly Lys Asn Lys Tyr Lys Thr Val Ile Gly Val Asn  
 45 385 390 395 400  
 Val Phe Val Gly Ser Asn Ser Thr Ile Ile Ala Pro Val Glu Leu Gly  
 405 410 415  
 50 Asp Asn Ser Leu Val Gly Ala Gly Ser Thr Ile Thr Lys Asp Val Pro  
 420 425 430  
 Ala Asp Ala Ile Ala Ile Gly Arg Gly Arg Gln Ile Asn Lys Asp Glu  
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 55 Tyr Ala Thr Arg Leu Pro His His Pro Lys Asn Gln  
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 <213> Streptococcus pneumoniae  
  
 <400> 196  
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                     20                    25                    30  
 15 Leu Asp Thr Glu Ala Val Ala Leu Gly Thr Pro Asn Glu Glu Thr Ala  
                     35                    40                    45  
 Phe Val Leu Asn Tyr Phe Gly Val Glu Ala Pro Arg Val Ile Thr Ser  
                     50                    55                    60  
 20 Ala Lys Ala Glu Gly Ala Glu Gln Val Ile Leu Thr Asp His Asn Glu  
                     65                    70                    75                    80  
 Phe Gln Gln Ser Val Ser Asp Ile Ala Glu Val Glu Val Tyr Gly Val  
 25                    85                    90                    95  
 Val Asp His His Arg Val Ala Asn Phe Glu Thr Ala Ser Pro Leu Tyr  
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 30 Met Arg Leu Glu Pro Val Gly Ser Ala Ser Ser Ile Val Tyr Arg Met  
                     115                    120                    125  
 Phe Lys Glu His Gly Val Ala Val Pro Lys Glu Ile Ala Gly Leu Met  
                     130                    135                    140  
 35 Leu Ser Gly Leu Ile Ser Asp Thr Leu Leu Leu Lys Ser Pro Thr Thr  
                     145                    150                    155                    160  
 His Pro Thr Asp Lys Ile Ile Ala Pro Glu Leu Ala Glu Leu Ala Gly  
 40                    165                    170                    175  
 Val Asn Leu Glu Glu Tyr Gly Leu Ala Met Leu Lys Ala Gly Thr Asn  
                     180                    185                    190  
 45 Leu Ala Ser Lys Ser Ala Glu Glu Leu Ile Asp Ile Asp Ala Lys Thr  
                     195                    200                    205  
 Phe Glu Leu Asn Gly Asn Asn Val Arg Val Ala Gln Val Asn Thr Val  
                     210                    215                    220  
 50 Asp Ile Ala Glu Val Leu Glu Arg Gln Ala Glu Ile Glu Ala Ala Met  
                     225                    230                    235                    240  
 Gln Ala Ala Asn Glu Ser Asn Gly Tyr Ser Asp Phe Val Leu Met Ile  
 55                    245                    250                    255  
 Thr Asp Ile Val Asn Ser Asn Ser Glu Ile Leu Ala Leu Gly Ala Asn

142

Val Leu Val Asp Lys Ile Gln Ala Ile Lys Glu Val Leu His Val Ser  
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 5 225  
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 <211> 161  
 10 <212> PRT  
 <213> Streptococcus pneumoniae  
 <400> 198  
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 20 20 25 30  
 Ser Lys Asn Glu Ala Arg Pro Val Pro Glu Val Ala Thr Gln Val Ala  
 35 40 45  
 Pro Ala Pro Val Leu Ala Thr Pro Ser Pro Val Ala Pro Thr Ser Ala  
 50 55 60  
 25 Pro Ala Glu Thr Val Ala Glu Glu Val Pro Ala Pro Ala Glu Ala Ser  
 65 70 75 80  
 Val Ala Ser Glu Gly Asn Leu Val Glu Ser Pro Leu Val Gly Val Val  
 30 85 90 95  
 Tyr Leu Ala Ala Gly Pro Asp Lys Pro Ala Phe Val Thr Val Gly Asp  
 100 105 110  
 35 Ser Val Lys Lys Gly Gln Thr Leu Val Ile Ile Glu Ala Met Lys Val  
 115 120 125  
 Met Asn Glu Ile Pro Ala Pro Lys Asp Gly Val Val Thr Glu Ile Leu  
 130 135 140  
 40 Val Ser Asn Glu Glu Met Val Glu Phe Gly Lys Gly Leu Val Arg Ile  
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 <210> 199  
 <211> 411  
 50 <212> PRT  
 <213> Streptococcus pneumoniae  
 <400> 199  
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 35 40 45  
 5 His Asn Ala Ala Glu Ile Gln Asp Phe Pro Phe Asp Lys Tyr Phe Val  
 50 55 60  
 10 Lys Lys Asp Thr Asn Arg Phe Asp Asn Tyr Ser Leu Tyr Ala Leu Tyr  
 65 70 75 80  
 Ala Ala Gln Glu Ala Val Asn His Ala Asn Leu Asp Val Glu Ala Leu  
 85 90 95  
 15 Asn Arg Asp Arg Phe Gly Val Ile Val Ala Ser Gly Ile Gly Gly Ile  
 100 105 110  
 Lys Glu Ile Glu Asp Gln Val Leu Arg Leu His Glu Lys Gly Pro Lys  
 115 120 125  
 20 Arg Val Lys Pro Met Thr Leu Pro Lys Ala Leu Pro Asn Met Ala Ser  
 130 135 140  
 Gly Asn Val Ala Met Arg Phe Gly Ala Asn Gly Val Cys Lys Ser Ile  
 145 150 155 160  
 Asn Thr Ala Cys Ser Ser Ser Asn Asp Ala Ile Gly Asp Ala Phe Arg  
 165 170 175  
 30 Ser Ile Lys Phe Gly Phe Gln Asp Val Met Leu Val Gly Gly Thr Glu  
 180 185 190  
 Ala Ser Ile Thr Pro Phe Ala Ile Ala Gly Phe Gln Ala Leu Thr Ala  
 195 200 205  
 35 Leu Ser Thr Thr Glu Asp Pro Thr Arg Ala Ser Ile Pro Phe Asp Lys  
 210 215 220  
 Asp Arg Asn Gly Phe Val Met Gly Glu Gly Ser Gly Met Leu Val Leu  
 225 230 235 240  
 Glu Ser Leu Glu His Ala Glu Lys Arg Gly Ala Thr Ile Leu Ala Glu  
 245 250 255  
 45 Val Val Gly Tyr Gly Asn Thr Cys Asp Ala Tyr His Met Thr Ser Pro  
 260 265 270  
 His Pro Glu Gly Gln Gly Ala Ile Lys Ala Ile Lys Leu Ala Leu Glu  
 275 280 285  
 50 Glu Ala Glu Ile Ser Pro Glu Gln Val Ala Tyr Val Asn Ala His Gly  
 290 295 300  
 Thr Ser Thr Pro Ala Asn Glu Lys Gly Glu Ser Gly Ala Ile Val Ala  
 305 310 315 320  
 Val Leu Gly Lys Glu Val Pro Val Ser Ser Thr Lys Ser Phe Thr Gly

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Leu Lys Tyr Glu Ser Gly Ala His Arg Val Gln Arg Val Pro Val Thr  
 180 185 190  
 5 Glu Ser Gln Gly Arg Val His Thr Ser Thr Ala Thr Val Leu Val Met  
 195 200 205  
 Pro Glu Val Glu Glu Val Glu Tyr Asp Ile Asp Pro Lys Asp Leu Arg  
 210 215 220  
 10 Val Asp Ile Tyr His Ala Ser Gly Ala Gly Gly Gln Asn Val Asn Lys  
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 Val Ala Thr Ala Val Arg Ile Val His Leu Pro Thr Asn Ile Lys Val  
 245 250 255  
 15 Glu Met Gln Glu Glu Arg Thr Gln Gln Lys Asn Arg Glu Lys Ala Met  
 260 265 270  
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 275 280 285  
 Asp Glu Gln Asp Ala Glu Arg Lys Ser Thr Ile Gly Thr Gly Asp Arg  
 290 295 300  
 25 Ser Glu Arg Ile Arg Thr Tyr Asn Phe Pro Gln Asn Arg Val Thr Asp  
 305 310 315 320  
 His Arg Ile Gly Leu Thr Leu Gln Lys Leu Asp Thr Ile Leu Ser Gly  
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 50 Glu Ile Ile Ile Val Asp Ala Gly Ile Lys Phe Pro Glu Asp Asp Leu  
 35 40 45  
 Leu Gly Ile Asp Tyr Val Ile Pro Asp Tyr Ser Tyr Ile Val Asp Asn  
 50 55 60  
 55 Ile Asp Arg Val Lys Ala Val Leu Ile Thr His Gly His Glu Asp His  
 65 70 75 80

Ile Gly Gly Ile Pro Phe Leu Leu Lys Gln Ala Asn Val Pro Ile Tyr  
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 5 Ala Gly Pro Leu Ala Leu Ala Leu Ile Arg Gly Lys Leu Glu Glu His  
                                     100                                    105                                    110  
 Gly Leu Leu Arg Asn Ala Lys Leu Tyr Glu Ile Asn His Asn Thr Glu  
                                     115                                    120                                    125  
 10 Leu Thr Phe Lys Asn Leu Lys Ala Thr Phe Phe Arg Thr Thr His Ser  
                                     130                                    135                                    140  
 15 Ile Pro Glu Pro Leu Gly Ile Val Ile His Thr Pro Gln Gly Lys Ile  
                                     145                                    150                                    155                                    160  
 Val Cys Thr Gly Asp Phe Lys Phe Asp Phe Thr Pro Val Gly Glu Pro  
                                     165                                    170                                    175  
 20 Ala Asp Leu His Arg Met Ala Ala Leu Gly Glu Glu Gly Val Leu Cys  
                                     180                                    185                                    190  
 Leu Leu Ser Asp Ser Thr Asn Ala Glu Val Pro Thr Phe Thr Asn Ser  
                                     195                                    200                                    205  
 25 Glu Lys Val Val Gly Gln Ser Ile Met Lys Ile Ile Gln Gly Ile Glu  
                                     210                                    215                                    220  
 Gly Arg Ile Ile Phe Ala Ser Phe Ala Ser Asn Ile Phe Arg Leu Gln  
                                     225                                    230                                    235                                    240  
 Gln Ala Thr Glu Ala Ala Val Lys Thr Gly Arg Lys Ile Ala Val Phe  
                                     245                                    250                                    255  
 35 Gly Arg Ser Met Glu Lys Ala Ile Val Asn Gly Ile Asp Leu Gly Tyr  
                                     260                                    265                                    270  
 Ile Lys Ala Pro Lys Gly Thr Phe Ile Glu Pro Asn Glu Ile Lys Asp  
                                     275                                    280                                    285  
 40 Tyr Pro Ala Gly Glu Val Leu Ile Leu Cys Thr Gly Ser Gln Gly Glu  
                                     290                                    295                                    300  
 Pro Met Ala Ala Leu Ser Arg Ile Ala Asn Gly Thr His Arg Gln Val  
                                     305                                    310                                    315                                    320  
 Gln Leu Gln Pro Gly Asp Thr Val Ile Phe Ser Ser Ser Pro Ile Pro  
                                     325                                    330                                    335  
 50 Gly Asn Thr Thr Ser Val Asn Lys Leu Ile Asn Ile Ile Ser Glu Ala  
                                     340                                    345                                    350  
 Gly Val Glu Val Ile His Gly Lys Val Asn Asn Ile His Thr Ser Gly  
                                     355                                    360                                    365  
 55 His Gly Gly Gln Gln Glu Gln Lys Leu Met Leu Cys Leu Ile Lys Pro  
                                     370                                    375                                    380

Lys Tyr Phe Met Pro Val His Gly Glu Tyr Arg Met Gln Lys Val His  
 385 390 395 400  
 5 Ala Gly Leu Ala Val Asp Thr Gly Val Glu Lys Asp Asn Ile Phe Ile  
 405 410 415  
 Met Ser Asn Gly Asp Val Leu Ala Leu Thr Ala Asp Ser Ala Arg Ile  
 420 425 430  
 10 Ala Gly His Phe Asn Ala Gln Asp Ile Tyr Val Asp Gly Asn Arg Ile  
 435 440 445  
 Gly Glu Ile Gly Ala Ala Val Leu Lys Asp Arg Arg Asp Leu Ser Glu  
 15 450 455 460  
 Asp Gly Val Val Leu Ala Val Ala Thr Val Asp Phe Lys Ser Gln Met  
 465 470 475 480  
 20 Ile Leu Ser Gly Pro Asp Ile Leu Ser Arg Gly Phe Val Tyr Met Arg  
 485 490 495  
 Glu Ser Gly Asp Leu Ile Arg Gln Ser Gln Arg Ile Leu Phe Asn Ala  
 500 505 510  
 25 Ile Arg Ile Ala Leu Lys Asn Lys Asp Ala Ser Val Gln Ser Val Asn  
 515 520 525  
 Gly Ala Ile Val Asn Ala Ile Arg Pro Phe Leu Tyr Glu Asn Thr Glu  
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 Met Ala Glu Val Glu Glu Leu Arg Val Gln Pro Gln Asp Ile Leu Ala  
 1 5 10 15  
 45 Glu Gln Ser Val Leu Gly Ala Ile Phe Ile Asp Glu Ser Lys Leu Val  
 20 25 30  
 Phe Val Arg Glu Tyr Ile Glu Ser Arg Asp Phe Phe Lys Tyr Ala His  
 35 40 45  
 50 Arg Leu Ile Phe Gln Ala Met Val Asp Leu Ser Asp Arg Gly Asp Ala  
 50 55 60  
 55 Ile Asp Ala Thr Thr Val Arg Thr Ile Leu Asp Asn Gln Gly Asp Leu  
 65 70 75 80  
 Gln Asn Ile Gly Gly Leu Ser Tyr Leu Val Glu Ile Val Asn Ser Val



	85	90	95
	Pro Thr Ser Ala Asn Ala Glu Tyr Tyr Ala Lys Ile Val Ala Glu Lys		
	100	105	110
5	Ala Met Leu Arg Arg Leu Ile Ala Lys Leu Thr Glu Ser Val Asn Gln		
	115	120	125
10	Ala Tyr Glu Ala Ser Gln Pro Ala Asp Glu Ile Ile Ala Gln Ala Glu		
	130	135	140
	Lys Gly Leu Ile Asp Val Ser Glu Asn Ala Asn Arg Ser Gly Phe Lys		
	145	150	155
15	Asn Ile Arg Asp Val Leu Asn Leu Asn Phe Gly Asn Leu Glu Ala Arg		
	165	170	175
	Ser Gln Gln Thr Thr Asp Ile Thr Gly Ile Ala Thr Gly Tyr Arg Asp		
	180	185	190
20	Leu Asp His Met Thr Thr Gly Leu His Glu Glu Glu Leu Ile Ile Leu		
	195	200	205
	Ala Ala Arg Pro Ala Val Gly Lys Thr Ala Phe Ala Leu Asn Ile Ala		
	210	215	220
25	Gln Asn Ile Gly Thr Lys Leu Asp Lys Thr Val Ala Ile Phe Ser Leu		
	225	230	235
	Glu Met Gly Ala Glu Ser Leu Val Asp Arg Met Leu Ala Ala Glu Gly		
	245	250	255
30	Leu Val Glu Ser His Ser Ile Arg Thr Gly Gln Leu Thr Asp Glu Glu		
	260	265	270
35	Trp Gln Lys Tyr Thr Ile Ala Gln Gly Asn Leu Ala Asn Ala Ser Ile		
	275	280	285
	Tyr Ile Asp Asp Thr Pro Gly Ile Arg Ile Thr Glu Ile Arg Ser Arg		
	290	295	300
40	Ser Arg Lys Leu Ala Gln Glu Thr Gly Asn Leu Gly Leu Ile Val Ile		
	305	310	315
	Asp Tyr Leu Gln Leu Ile Thr Gly Thr Gly Arg Glu Asn Arg Gln Gln		
	325	330	335
45	Glu Val Ser Glu Ile Ser Arg Gln Leu Lys Ile Leu Ala Lys Glu Leu		
	340	345	350
50	Lys Val Pro Val Ile Ala Leu Ser Gln Leu Ser Arg Gly Val Glu Gln		
	355	360	365
	Arg Gln Asp Lys Arg Pro Val Leu Ser Asp Ile Arg Glu Ser Gly Ser		
	370	375	380
55	Ile Glu Gln Asp Ala Asp Ile Val Ala Phe Leu Tyr Arg Asp Asp Tyr		

150

Ile Asn Ala Phe Gln Pro Glu Glu Tyr Trp Thr Val Asp Ala Val Phe  
 195 200 205  
 5 Lys Lys Gly Thr Lys Gln Phe His Ala Ser Phe Tyr Gly Val Asp Gly  
 210 215 220  
 Lys Lys Met Lys Leu Thr Ser Asn Asn Glu Val Lys Glu Val Leu Ser  
 225 230 235 240  
 10 Arg Leu Thr Ser Lys Asp Phe Ser Val Asp Gln Val Asp Lys Lys Glu  
 245 250 255  
 Arg Lys Arg Asn Ala Pro Leu Pro Tyr Thr Thr Ser Ser Met Gln Met  
 260 265 270  
 15 Asp Ala Ala Asn Lys Ile Asn Phe Arg Thr Arg Lys Thr Met Met Val  
 275 280 285  
 Ala Gln Gln Leu Tyr Glu Gly Ile Asn Ile Gly Ser Gly Val Gln Gly  
 290 295 300  
 Leu Ile Thr Tyr Met Arg Thr Asp Ser Thr Arg Ile Ser Pro Val Ala  
 305 310 315 320  
 25 Gln Asn Glu Ala Ala Ser Phe Ile Thr Asp Arg Phe Gly Ser Lys Tyr  
 325 330 335  
 Ser Lys His Gly Ser Lys Val Lys Asn Ala Ser Gly Ala Gln Asp Ala  
 340 345 350  
 30 His Glu Ala Ile Arg Pro Ser Ser Val Phe Asn Thr Pro Glu Ser Ile  
 355 360 365  
 Ala Lys Tyr Leu Asp Lys Asp Gln Leu Lys Leu Tyr Thr Leu Ile Trp  
 370 375 380  
 Asn Arg Phe Val Ala Ser Gln Met Thr Ala Ala Val Phe Asp Thr Met  
 385 390 395 400  
 40 Ala Val Lys Leu Ser Gln Lys Gly Val Gln Phe Ala Ala Asn Gly Ser  
 405 410 415  
 Gln Val Lys Phe Asp Gly Tyr Leu Ala Ile Tyr Asn Asp Ser Asp Lys  
 420 425 430  
 45 Asn Lys Met Leu Pro Asp Met Val Val Gly Asp Val Val Lys Gln Val  
 435 440 445  
 Asn Ser Lys Pro Glu Gln His Phe Thr Gln Pro Pro Ala Arg Tyr Ser  
 450 455 460  
 Glu Ala Thr Leu Ile Lys Thr Leu Glu Glu Asn Gly Val Gly Arg Pro  
 465 470 475 480  
 55 Ser Thr Tyr Ala Pro Thr Ile Glu Thr Ile Gln Lys Arg Tyr Tyr Val  
 485 490 495

Arg Leu Ala Ala Lys Arg Phe Glu Pro Thr Glu Leu Gly Glu Ile Val  
 500 505 510  
 5 sn Lys Leu Ile Val Glu Tyr Phe Pro Asp Ile Val Asn Val Thr Phe  
 515 520 525  
 Thr Ala Glu Met Glu Gly Lys Leu Asp Asp Val Glu Val Gly Lys Glu  
 530 535 540  
 10 Gln Trp Arg Arg Val Ile Asp Ala Phe Tyr Lys Pro Phe Ser Lys Glu  
 545 550 555 560  
 15 Val Ala Lys Ala Glu Glu Glu Met Glu Lys Ile Gln Ile Lys Asp Glu  
 565 570 575  
 Pro Ala Gly Phe Asp Cys Glu Val Cys Gly Ser Pro Met Val Ile Lys  
 580 585 590  
 20 Leu Gly Arg Phe Gly Lys Phe Tyr Ala Cys Ser Asn Phe Pro Asp Cys  
 595 600 605  
 Arg His Thr Gln Ala Ile Val Lys Glu Ile Gly Val Glu Cys Pro Ser  
 610 615 620  
 25 Cys His Gln Gly Gln Ile Ile Glu Arg Lys Thr Lys Arg Asn Arg Leu  
 625 630 635 640  
 30 Phe Tyr Gly Cys Asn Arg Tyr Pro Glu Cys Glu Phe Thr Ser Trp Asp  
 645 650 655  
 Lys Pro Val Gly Arg Asp Cys Pro Lys Cys Gly Asn Phe Leu Met Glu  
 660 665 670  
 35 Lys Lys Val Arg Gly Gly Gly Lys Gln Val Val Cys Ser Lys Gly Asp  
 675 680 685  
 Tyr Glu Glu Glu Lys Met Ala Leu Cys Gln Leu  
 690 695  
 40  
 <210> 204  
 <211> 326  
 <212> PRT  
 45 <213> Streptococcus pneumoniae  
 <400> 204  
 Met Phe Ile Ser Ile Ser Ala Gly Ile Val Thr Phe Leu Leu Thr Leu  
 1 5 10 15  
 50 Val Gly Ile Pro Ala Phe Ile Gln Phe Tyr Arg Lys Ala Gln Ile Thr  
 20 25 30  
 Gly Gln Gln Met His Glu Asp Val Lys Gln His Gln Ala Lys Ala Gly  
 35 40 45  
 55 Thr Pro Thr Met Gly Gly Leu Val Phe Leu Ile Thr Ser Val Leu Val

50                      55                      60  
 Ala Phe Phe Phe Ala Leu Phe Ser Ser Gln Phe Ser Asn Asn Val Gly  
 65                      70                      75                      80  
 5 Met Ile Leu Phe Ile Leu Val Leu Tyr Gly Leu Val Gly Phe Leu Asp  
                                  85                      90                      95  
 10 Asp Phe Leu Lys Val Phe Arg Lys Ile Asn Glu Gly Leu Asn Pro Lys  
                                  100                      105                      110  
                                  Gln Lys Leu Ala Leu Gln Leu Leu Gly Gly Val Ile Phe Tyr Leu Phe  
                                  115                      120                      125  
 15 Tyr Glu Arg Gly Gly Asp Met Leu Ser Val Phe Gly Tyr Gln Val His  
                                  130                      135                      140  
                                  Leu Gly Ile Phe Tyr Ile Val Phe Ala Leu Phe Trp Leu Val Gly Phe  
 20 145                      150                      155                      160  
                                  Ser Asn Ala Val Asn Leu Thr Asp Gly Val Asp Gly Leu Ala Ser Ile  
                                  165                      170                      175  
 25 Ser Val Val Ile Ser Leu Ser Ala Tyr Gly Val Ile Ala Tyr Val Gln  
                                  180                      185                      190  
                                  Gly Gln Met Asp Ile Leu Leu Val Ile Leu Ala Met Ile Gly Gly Leu  
                                  195                      200                      205  
 30 Leu Ser Phe Phe Ile Phe Asn His Lys Pro Ala Lys Ile Phe Met Gly  
                                  210                      215                      220  
                                  Asp Val Gly Ser Leu Ala Leu Gly Gly Met Leu Ala Ala Ile Ser Met  
 35 225                      230                      235                      240  
                                  Ala Leu His Gln Glu Trp Thr Leu Leu Ile Ile Gly Ile Val Tyr Val  
                                  245                      250                      255  
 40 Phe Glu Thr Thr Ser Val Met Met Gln Val Ser Tyr Phe Lys Leu Thr  
                                  260                      265                      270  
                                  Gly Gly Lys Arg Ile Phe Arg Met Thr Pro Val His His His Phe Glu  
                                  275                      280                      285  
 45 Leu Gly Gly Leu Ser Gly Lys Gly Asn Pro Trp Ser Glu Trp Lys Val  
                                  290                      295                      300  
                                  Asp Phe Phe Phe Trp Gly Val Gly Leu Leu Ala Ser Leu Leu Thr Leu  
 50 305                      310                      315                      320  
                                  Ala Ile Leu Tyr Leu Met  
                                  325  
 55 <210> 205  
                                  <211> 693  
                                  <212> PRT

&lt;213&gt; Streptococcus pneumoniae

&lt;400&gt; 205

5 Met Ala Arg Glu Phe Ser Leu Glu Lys Thr Arg Asn Ile Gly Ile Met  
 1 5 10 15  
 Ala His Val Asp Ala Gly Lys Thr Thr Thr Thr Glu Arg Ile Leu Tyr  
 20 25 30  
 10 Tyr Thr Gly Lys Ile His Lys Ile Gly Glu Thr His Glu Gly Ala Ser  
 35 40 45  
 Gln Met Asp Trp Met Glu Gln Glu Gln Glu Arg Gly Ile Thr Ile Thr  
 50 55 60  
 15 Ser Ala Ala Thr Thr Ala Gln Trp Asn Asn His Arg Val Asn Ile Ile  
 65 70 75 80  
 20 Asp Thr Pro Gly His Val Asp Phe Thr Ile Glu Val Gln Arg Ser Leu  
 85 90 95  
 Arg Val Leu Asp Gly Ala Val Thr Val Leu Asp Ser Gln Ser Gly Val  
 100 105 110  
 25 Glu Pro Gln Thr Glu Thr Val Trp Arg Gln Ala Thr Glu Tyr Gly Val  
 115 120 125  
 Pro Arg Ile Val Phe Ala Asn Lys Met Asp Lys Ile Gly Ala Asp Phe  
 130 135 140  
 30 Leu Tyr Ser Val Ser Thr Leu His Asp Arg Leu Gln Ala Asn Ala His  
 145 150 155 160  
 35 Pro Ile Gln Leu Pro Ile Gly Ser Glu Asp Asp Phe Arg Gly Ile Ile  
 165 170 175  
 Asp Leu Ile Lys Met Lys Ala Glu Ile Tyr Thr Asn Asp Leu Gly Thr  
 180 185 190  
 40 Asp Ile Leu Glu Glu Asp Ile Pro Ala Glu Tyr Leu Asp Gln Ala Gln  
 195 200 205  
 Glu Tyr Arg Glu Lys Leu Ile Glu Ala Val Ala Glu Thr Asp Glu Glu  
 210 215 220  
 45 Leu Met Met Lys Tyr Leu Glu Gly Glu Glu Ile Thr Asn Glu Glu Leu  
 225 230 235 240  
 50 Lys Ala Gly Ile Arg Lys Ala Thr Ile Asn Val Glu Phe Phe Pro Val  
 245 250 255  
 Leu Cys Gly Ser Ala Phe Lys Asn Lys Gly Val Gln Leu Met Leu Asp  
 260 265 270  
 55 Ala Val Ile Asp Tyr Leu Pro Ser Pro Leu Asp Ile Pro Ala Ile Lys  
 275 280 285

Gly Ile Asn Pro Asp Thr Asp Ala Glu Glu Ile Arg Pro Ala Ser Asp  
 290 295 300  
 5 Glu Glu Pro Phe Ala Ala Leu Ala Phe Lys Ile Met Thr Asp Pro Phe  
 305 310 315 320  
 Val Gly Arg Leu Thr Phe Phe Arg Val Tyr Ser Gly Val Leu Gln Ser  
 325 330 335  
 10 Gly Ser Tyr Val Leu Asn Thr Ser Lys Gly Lys Arg Glu Arg Ile Gly  
 340 345 350  
 Arg Ile Leu Gln Met His Ala Asn Ser Arg Gln Glu Ile Asp Thr Val  
 355 360 365  
 15 Tyr Ser Gly Asp Ile Ala Ala Ala Val Gly Leu Lys Asp Thr Thr Thr  
 370 375 380  
 20 Gly Asp Ser Leu Thr Asp Glu Lys Ala Lys Ile Ile Leu Glu Ser Ile  
 385 390 395 400  
 Asn Val Pro Glu Pro Val Ile Gln Leu Met Val Glu Pro Lys Ser Lys  
 405 410 415  
 25 Ala Asp Gln Asp Lys Met Gly Ile Ala Leu Gln Lys Leu Ala Glu Glu  
 420 425 430  
 Asp Pro Thr Phe Arg Val Glu Thr Asn Val Glu Thr Gly Glu Thr Val  
 435 440 445  
 30 Ile Ser Gly Met Gly Glu Leu His Leu Asp Val Leu Val Asp Arg Met  
 450 455 460  
 35 Arg Arg Glu Phe Lys Val Glu Ala Asn Val Gly Ala Pro Gln Val Ser  
 465 470 475 480  
 Tyr Arg Glu Thr Phe Arg Ala Ser Thr Gln Ala Arg Gly Phe Phe Lys  
 485 490 495  
 40 Arg Gln Ser Gly Gly Lys Gly Gln Phe Gly Asp Val Trp Ile Glu Phe  
 500 505 510  
 Thr Pro Asn Glu Glu Gly Lys Gly Phe Glu Phe Glu Asn Ala Ile Val  
 515 520 525  
 45 Gly Gly Val Val Pro Arg Glu Phe Ile Pro Ala Val Glu Lys Gly Leu  
 530 535 540  
 50 Val Glu Ser Met Ala Asn Gly Val Leu Ala Gly Tyr Pro Met Val Asp  
 545 550 555 560  
 Val Lys Ala Lys Leu Tyr Asp Gly Ser Tyr His Asp Val Asp Ser Ser  
 565 570 575  
 55 Glu Thr Ala Phe Lys Ile Ala Ala Ser Leu Ser Leu Lys Glu Ala Ala  
 580 585 590

Lys Ser Ala Gln Pro Ala Ile Leu Glu Pro Met Met Leu Val Thr Ile  
 595 600 605  
 5 Thr Val Pro Glu Glu Asn Leu Gly Asp Val Met Gly His Val Thr Ala  
 610 615 620  
 Arg Arg Gly Arg Val Asp Gly Met Glu Ala His Gly Asn Ser Gln Ile  
 625 630 635 640  
 10 Val Arg Ala Tyr Val Pro Leu Ala Glu Met Phe Gly Tyr Ala Thr Val  
 645 650 655  
 Leu Arg Ser Ala Ser Gln Gly Arg Gly Thr Phe Met Met Val Phe Asp  
 660 665 670  
 15 His Tyr Glu Asp Val Pro Lys Ser Val Gln Glu Glu Ile Ile Lys Lys  
 675 680 685  
 20 Asn Lys Gly Glu Asp  
 690  
 <210> 206  
 <211> 408  
 25 <212> PRT  
 <213> Streptococcus pneumoniae  
 <400> 206  
 30 Met Pro Asn Tyr Asn Ile Pro Phe Ser Pro Pro Asp Ile Thr Glu Ala  
 1 5 10 15  
 Glu Ile Ala Glu Val Ala Asp Thr Leu Arg Ser Gly Trp Ile Thr Thr  
 20 25 30  
 35 Gly Pro Lys Thr Lys Glu Leu Glu Arg Arg Leu Ser Leu Tyr Thr Gln  
 35 40 45  
 Thr Pro Lys Thr Val Cys Leu Asn Ser Ala Thr Ala Ala Leu Glu Leu  
 50 55 60  
 40 Ile Leu Arg Val Leu Glu Val Gly Pro Gly Asp Glu Val Ile Val Pro  
 65 70 75 80  
 45 Ala Met Thr Tyr Thr Ala Ser Cys Ser Val Ile Thr His Val Gly Ala  
 85 90 95  
 Thr Pro Val Met Val Asp Ile Gln Ala Asp Thr Phe Glu Met Asp Tyr  
 100 105 110  
 50 Asp Leu Leu Glu Gln Ala Ile Thr Glu Lys Thr Lys Val Ile Ile Pro  
 115 120 125  
 Val Glu Leu Ala Gly Ile Val Cys Asp Tyr Asp Arg Leu Phe Gln Val  
 130 135 140  
 55 Val Glu Lys Lys Arg Asp Phe Phe Thr Ala Ser Ser Lys Trp Gln Lys  
 145 150 155 160



Ala Phe Asn Arg Ile Val Ile Val Ser Asp Ser Ala His Ala Leu Gly  
 165 170 175

5 Ser Thr Tyr Lys Gly Gln Pro Ser Gly Ser Ile Ala Asp Phe Thr Ser  
 180 185 190

Phe Ser Phe His Ala Val Lys Asn Phe Thr Thr Ala Glu Gly Gly Ser  
 195 200 205

10 Ala Thr Trp Lys Ala Asn Pro Val Ile Asp Asp Glu Glu Met Tyr Lys  
 210 215 220

15 Glu Phe Gln Ile Leu Ser Leu His Gly Gln Thr Lys Asp Ala Leu Ala  
 225 230 235 240

Lys Met Gln Leu Gly Ser Trp Glu Tyr Asp Ile Val Thr Pro Ala Tyr  
 245 250 255

20 Lys Cys Asn Met Thr Asp Ile Met Ala Ser Leu Gly Leu Val Gln Leu  
 260 265 270

Asp Arg Tyr Pro Ser Leu Leu Gln Arg Arg Lys Asp Ile Val Asp Arg  
 275 280 285

25 Tyr Asp Ser Gly Phe Ala Gly Ser Arg Ile His Pro Leu Ala His Lys  
 290 295 300

30 Thr Glu Thr Val Glu Ser Ser Arg His Leu Tyr Ile Thr Arg Val Glu  
 305 310 315 320

Gly Ala Ser Leu Glu Glu Arg Ser Leu Ile Ile Gln Glu Leu Ala Lys  
 325 330 335

35 Ala Gly Ile Ala Ser Asn Val His Tyr Lys Pro Leu Pro Leu Leu Thr  
 340 345 350

Ala Tyr Lys Asn Leu Gly Phe Asp Met Thr Asn Tyr Pro Lys Ala Tyr  
 355 360 365

40 Ala Phe Phe Glu Asn Glu Ile Thr Leu Pro Leu His Thr Lys Leu Ser  
 370 375 380

45 Asp Glu Glu Val Asp Tyr Ile Ile Glu Thr Phe Lys Thr Val Ser Glu  
 385 390 395 400

Lys Val Leu Thr Leu Ser Lys Lys  
 405

50  
 <210> 207  
 <211> 325  
 <212> PRT  
 <213> Streptococcus pneumoniae

55  
 <400> 207  
 Met Thr Glu Pro Asp Phe Trp Asn Asp Asn Ile Ala Ala Gln Lys Thr

1                      5                      10                      15  
 Ser Gln Glu Leu Asn Val Phe Lys Asn Thr Tyr Asn Thr Phe His Lys  
                          20                      25                      30  
 5 Met Glu Glu Leu Gln Asp Glu Val Glu Ile Leu Leu Asp Phe Leu Ala  
                          35                      40                      45  
 10 Glu Asp Glu Ser Val His Asp Glu Leu Val Ala Gln Leu Ala Glu Leu  
                          50                      55                      60  
 Asp Lys Ile Met Thr Ser Tyr Glu Met Thr Leu Leu Leu Ser Glu Pro  
                          65                      70                      75                      80  
 15 Tyr Asp His Asn Asn Ala Ile Leu Glu Ile His Pro Gly Ser Gly Gly  
    85                      90                      95  
 Thr Glu Ala Gln Asp Trp Gly Asp Met Leu Leu Arg Met Tyr Thr Arg  
    100                      105                      110  
 20 Tyr Gly Asn Ala Lys Gly Phe Lys Val Glu Val Leu Asp Tyr Gln Ala  
    115                      120                      125  
 25 Gly Asp Glu Ala Gly Ile Lys Ser Val Thr Leu Ser Phe Glu Gly Pro  
    130                      135                      140  
 Asn Ala Tyr Gly Leu Leu Lys Ser Glu Met Gly Val His Arg Leu Val  
    145                      150                      155                      160  
 30 Arg Ile Ser Pro Phe Asp Ser Ala Lys Arg Arg His Thr Ser Phe Thr  
    165                      170                      175  
 Ser Val Glu Val Met Pro Glu Leu Asp Asp Thr Ile Glu Val Glu Ile  
    180                      185                      190  
 35 Arg Glu Asp Asp Ile Lys Met Asp Thr Phe Arg Ser Gly Gly Ala Gly  
    195                      200                      205  
 40 Gly Gln Asn Val Asn Lys Val Ser Thr Gly Val Arg Leu Thr His Ile  
    210                      215                      220  
 Pro Thr Gly Ile Val Val Gln Ser Thr Val Asp Arg Thr Gln Tyr Gly  
    225                      230                      235                      240  
 45 Asn Arg Asp Arg Ala Met Lys Met Leu Gln Ala Lys Leu Tyr Gln Met  
    245                      250                      255  
 Glu Gln Glu Lys Lys Ala Ala Glu Val Asp Ser Leu Lys Gly Glu Lys  
    260                      265                      270  
 50 Lys Glu Ile Thr Trp Gly Ser Gln Ile Arg Ser Tyr Val Phe Thr Pro  
    275                      280                      285  
 55 Tyr Thr Met Val Lys Asp His Arg Thr Ser Phe Glu Val Ala Gln Val  
    290                      295                      300  
 Asp Lys Val Met Asp Gly Asp Leu Asp Gly Phe Ile Asp Ala Tyr Leu

305                                      310                                      315                                      320  
 Lys Trp Arg Ile Ser  
    325  
 5  
 <210> 208  
 <211> 249  
 <212> PRT  
 10 <213> Streptococcus pneumoniae  
 <400> 208  
 Met Phe Tyr Thr Tyr Leu Arg Gly Leu Val Val Leu Leu Leu Trp Ser  
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 15 Ile Asn Gly Asn Ala His Tyr His Asn Thr Asp Lys Ile Pro Asn Gln  
   20  25  30  
 20 Asp Glu Asn Tyr Ile Leu Val Ala Pro His Arg Thr Trp Trp Asp Pro  
   35  40  45  
 Val Tyr Met Ala Phe Ala Thr Lys Pro Lys Gln Phe Ile Phe Met Ala  
   50  55  60  
 25 Lys Lys Glu Leu Phe Thr Asn Arg Ile Phe Gly Trp Trp Ile Arg Met  
   65  70  75  80  
 Cys Gly Ala Phe Pro Ile Asp Arg Glu Asn Pro Ser Ala Ser Ala Ile  
   85  90  95  
 30 Lys Tyr Pro Ile Asn Val Leu Lys Lys Ser Asp Arg Ser Leu Ile Met  
   100  105  110  
 35 Phe Pro Ser Gly Ser Arg His Ser Asn Asp Val Lys Gly Gly Ala Ala  
   115  120  125  
 Leu Ile Ala Lys Met Ala Lys Val Arg Ile Met Pro Val Thr Tyr Thr  
   130  135  140  
 40 Gly Pro Met Thr Leu Lys Gly Leu Ile Ser Arg Glu Arg Val Asp Met  
   145  150  155  160  
 Asn Phe Gly Asn Pro Ile Asp Ile Ser Asp Ile Lys Lys Met Asn Asp  
   165  170  175  
 45 Glu Gly Ile Glu Thr Val Ala Asn Arg Ile Gln Thr Glu Phe Gln Arg  
   180  185  190  
 50 Leu Asp Glu Glu Thr Lys Gln Trp His Asn Asp Lys Lys Pro Asn Pro  
   195  200  205  
 Leu Trp Trp Phe Ile Arg Ile Pro Ala Leu Ile Leu Ala Ile Ile Leu  
   210  215  220  
 55 Ala Ile Leu Thr Ile Ile Phe Ser Phe Ile Ala Ser Phe Ile Trp Asn  
   225  230  235  240

Pro Asp Lys Lys Arg Glu Glu Leu Ala  
245

- 5 <210> 209  
<211> 1033  
<212> PRT  
<213> Streptococcus pneumoniae
- 10 <400> 209  
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1 5 10 15  
Val Ile Ser Ile Glu Lys Tyr Val Arg Ala Ala Lys Glu Tyr Gly Tyr  
15 20 25 30  
Thr His Leu Ala Met Met Asp Ile Asp Asn Leu Tyr Gly Ala Phe Asp  
35 40 45  
20 Phe Leu Glu Ile Thr Lys Lys Tyr Gly Ile His Pro Leu Leu Gly Leu  
50 55 60  
Glu Met Thr Val Phe Val Asp Asp Gln Gly Val Asn Leu Arg Phe Leu  
65 70 75 80  
25 Ala Leu Ser Ser Val Gly Tyr Gln Gln Leu Met Lys Leu Ser Thr Ala  
85 90 95  
30 Lys Met Gln Gly Glu Lys Thr Trp Ser Val Leu Ser Gln Tyr Leu Glu  
100 105 110  
Asp Ile Ala Val Ile Val Pro Tyr Phe Asp Arg Val Glu Ser Leu Glu  
115 120 125  
35 Leu Gly Cys Asp Tyr Tyr Ile Gly Val Tyr Pro Glu Thr Leu Ala Ser  
130 135 140  
Glu Phe His His Pro Ile Leu Pro Leu Tyr Arg Val Asn Ala Phe Glu  
145 150 155 160  
40 Ser Arg Asp Arg Glu Val Leu Gln Val Leu Thr Ala Ile Lys Glu Asn  
165 170 175  
45 Leu Pro Leu Arg Glu Val Pro Leu Arg Ser Arg Gln Asp Val Phe Ile  
180 185 190  
Ser Ala Ser Ser Leu Glu Lys Leu Phe Gln Glu Arg Phe Pro Gln Ala  
195 200 205  
50 Leu Asp Asn Leu Glu Lys Leu Ile Ser Gly Ile Ser Tyr Asp Leu Asp  
210 215 220  
Thr Ser Leu Lys Leu Pro Arg Phe Asn Pro Ala Arg Pro Ala Val Glu  
225 230 235 240  
55 Glu Leu Arg Glu Arg Ala Glu Leu Gly Leu Val Gln Lys Gly Leu Thr  
245 250 255

Ser Lys Glu Tyr Gln Asp Arg Leu Asp Gln Glu Leu Ser Val Ile His  
 260 265 270  
 5 Asp Met Gly Phe Asp Asp Tyr Phe Leu Val Val Trp Asp Leu Leu Arg  
 275 280 285  
 Phe Gly Arg Ser Asn Gly Tyr Tyr Met Gly Met Gly Arg Gly Ser Ala  
 290 295 300  
 10 Val Gly Ser Leu Val Ser Tyr Ala Leu Asp Ile Thr Gly Ile Asp Pro  
 305 310 315 320  
 Val Glu Lys Asn Leu Ile Phe Glu Arg Phe Leu Asn Arg Glu Arg Tyr  
 15 325 330 335  
 Thr Met Pro Asp Ile Asp Ile Asp Ile Pro Asp Ile Tyr Arg Pro Asp  
 340 345 350  
 20 Phe Ile Arg Tyr Val Gly Asn Lys Tyr Gly Ser Lys His Ala Ala Gln  
 355 360 365  
 Ile Val Thr Phe Ser Thr Phe Gly Ala Lys Gln Ala Leu Arg Asp Val  
 370 375 380  
 25 Leu Lys Arg Phe Gly Val Pro Glu Tyr Glu Leu Ser Ala Ile Thr Lys  
 385 390 395 400  
 Lys Ile Ser Phe Arg Asp Asn Leu Lys Ser Ala Tyr Glu Gly Asn Leu  
 30 405 410 415  
 Gln Phe Arg Gln Gln Ile Asn Ser Lys Leu Glu Tyr Gln Lys Ala Phe  
 420 425 430  
 35 Glu Ile Ala Cys Lys Ile Glu Gly Tyr Pro Arg Gln Thr Ser Val His  
 435 440 445  
 Ala Ala Gly Val Val Ile Ser Asp Gln Asp Leu Thr Asn Tyr Ile Pro  
 40 450 455 460  
 Leu Lys Tyr Gly Asp Glu Ile Pro Leu Thr Gln Tyr Asp Ala His Gly  
 465 470 475 480  
 45 Val Glu Ala Ser Gly Leu Leu Lys Met Asp Phe Leu Gly Leu Arg Asn  
 485 490 495  
 Leu Thr Phe Val Gln Lys Met Gln Glu Leu Leu Ala Glu Ile Glu Gly  
 500 505 510  
 50 Ile His Leu Lys Ile Glu Glu Ile Asp Leu Glu Asp Lys Glu Thr Leu  
 515 520 525  
 Asp Leu Phe Ala Ser Gly Asn Thr Lys Gly Ile Phe Gln Phe Glu Gln  
 530 535 540  
 55 Pro Gly Ala Ile Arg Leu Leu Lys Arg Val Gln Pro Val Cys Phe Glu  
 545 550 555 560

Asp Val Val Ala Thr Thr Ser Leu Asn Arg Pro Gly Ala Ser Asp Tyr  
 565 570 575  
 5 Ile Asn Asn Phe Val Ala Arg Lys His Gly Gln Glu Glu Val Thr Val  
 580 585 590  
 Leu Asp Pro Val Leu Glu Asp Ile Leu Ala Pro Thr Tyr Gly Ile Met  
 595 600 605  
 10 Leu Tyr Gln Glu Gln Val Met Gln Val Ala Gln Arg Phe Ala Gly Phe  
 610 615 620  
 Ser Leu Gly Lys Ala Asp Ile Leu Arg Arg Ala Met Gly Lys Lys Asp  
 625 630 635 640  
 15 Ala Ser Ala Met His Glu Met Arg Ala Ser Phe Ile Gln Gly Ser Leu  
 645 650 655  
 20 Glu Ala Gly His Thr Val Glu Lys Ala Glu Gln Val Phe Asp Val Met  
 660 665 670  
 Glu Lys Phe Ala Gly Tyr Gly Phe Asn Arg Ser His Ala Tyr Ala Tyr  
 675 680 685  
 25 Ser Ala Leu Ala Phe Gln Leu Ala Tyr Phe Lys Thr His Tyr Pro Ala  
 690 695 700  
 30 Ile Phe Tyr Gln Ile Met Leu Asn Ser Ala Asn Ser Asp Tyr Leu Ile  
 705 710 715 720  
 Asp Ala Leu Glu Ala Gly Phe Glu Val Ala Pro Leu Ser Ile Asn Thr  
 725 730 735  
 35 Ile Pro Tyr His Asp Lys Ile Ala Asn Lys Ala Ile Tyr Leu Gly Leu  
 740 745 750  
 Lys Ser Ile Lys Gly Val Ser Asn Asp Leu Ala Leu Trp Ile Ile Glu  
 755 760 765  
 40 His Arg Pro Tyr Ser Asn Ile Glu Asp Phe Ile Ala Lys Leu Pro Glu  
 770 775 780  
 Asn Tyr Leu Lys Leu Pro Leu Leu Glu Pro Leu Val Lys Val Gly Leu  
 785 790 795 800  
 Phe Asp Ser Phe Glu Lys Asn Arg Gln Lys Val Phe Asn Asn Leu Ala  
 805 810 815  
 50 Asn Leu Phe Glu Phe Val Lys Glu Leu Gly Ser Leu Phe Gly Asp Ala  
 820 825 830  
 Ile Tyr Ser Trp Gln Glu Ser Glu Asp Trp Thr Glu Gln Glu Lys Phe  
 835 840 845  
 55 Tyr Met Glu Gln Glu Leu Leu Gly Ile Gly Val Ser Lys His Pro Leu  
 850 855 860

Gln Ala Ile Ala Ser Lys Ala Ile Tyr Pro Ile Thr Pro Ile Gly Asn  
 865 870 875 880  
 5 Leu Ser Glu Asn Ser Tyr Ala Ile Ile Leu Val Glu Val Gln Lys Ile  
 885 890 895  
 Lys Val Ile Arg Thr Lys Lys Gly Glu Asn Met Ala Phe Leu Gln Ala  
 900 905 910  
 10 Asp Asp Ser Lys Lys Lys Leu Asp Val Thr Leu Phe Ser Asp Leu Tyr  
 915 920 925  
 15 Arg Gln Val Gly Gln Glu Ile Lys Glu Gly Ala Phe Tyr Tyr Val Lys  
 930 935 940  
 Gly Lys Ile Gln Ser Arg Asp Gly Arg Leu Gln Met Ile Ala Gln Glu  
 945 950 955 960  
 20 Ile Arg Glu Ala Val Ala Glu Arg Phe Trp Ile Gln Val Lys Asn His  
 965 970 975  
 Glu Ser Asp Gln Glu Ile Ser Arg Ile Leu Glu Gln Phe Lys Gly Pro  
 980 985 990  
 25 Ile Pro Val Ile Ile Arg Tyr Glu Glu Glu Gln Lys Thr Ile Val Ser  
 995 1000 1005  
 30 Pro His His Phe Val Ala Lys Ser Asn Glu Leu Glu Glu Lys Leu Asn  
 1010 1015 1020  
 Glu Ile Val Met Lys Thr Ile Tyr Arg  
 1025 1030  
 35  
 <210> 210  
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 <212> PRT  
 <213> Streptococcus pneumoniae  
 40  
 <400> 210  
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 1 5 10 15  
 45 Gln Ser Leu His Arg Lys Thr Thr Pro Pro Leu Thr Glu Glu Glu Leu  
 20 25 30  
 Glu Ser Ile Lys Ser Phe Asn Asp Gln Ile Ser Leu Gln Asp Val Thr  
 35 40 45  
 50 Asp Ile Tyr Leu Pro Leu Ala His Leu Ile Gln Ile Tyr Lys Arg Thr  
 50 55 60  
 55 Lys Glu Asp Leu Ala Phe Ser Lys Gly Ile Phe Leu Gln Arg Glu Ser  
 65 70 75 80  
 Lys Ser Gln Pro Phe Ile Ile Gly Val Ser Gly Ser Val Ala Val Gly

85 90 95  
 Lys Ser Thr Thr Ser Arg Leu Leu Gln Ile Leu Leu Ser Arg Thr Phe  
 100 105 110  
 5 Thr Asp Ala Thr Val Glu Leu Val Thr Thr Asp Gly Phe Leu Tyr Pro  
 115 120 125  
 10 Asn Gln Thr Leu Ile Glu Gln Gly Ile Leu Asn Arg Lys Gly Phe Pro  
 130 135 140  
 Glu Ser Tyr Asp Met Glu Ala Leu Leu Asn Phe Leu Asp Arg Ile Lys  
 145 150 155 160  
 15 Asn Gly Gln Asp Val Asp Ile Pro Val Tyr Ser His Glu Val Tyr Asp  
 165 170 175  
 Ile Val Pro Lys Lys Lys Gln Ser Val Lys Ala Ala Asp Phe Val Ile  
 180 185 190  
 20 Val Glu Gly Ile Asn Val Phe Gln Asn Pro Gln Asn Asp Arg Leu Tyr  
 195 200 205  
 Ile Thr Asp Phe Phe Asp Phe Ser Ile Tyr Val Asp Ala Gly Val Asp  
 210 215 220  
 Asp Ile Glu Ser Trp Tyr Leu Asp Arg Phe Leu Lys Met Leu Ser Leu  
 225 230 235 240  
 30 Ala Gln Asn Asp Pro Asp Ser Tyr Tyr Tyr Arg Phe Thr Gln Met Pro  
 245 250 255  
 Ile Gly Glu Val Glu Ser Phe Ala His Gln Val Trp Thr Ser Ile Asn  
 260 265 270  
 35 Leu Thr Asn Leu Gln Asn Tyr Ile Glu Pro Thr Arg Asn Arg Ala Glu  
 275 280 285  
 Val Ile Leu His Lys Ser Lys Asn His Glu Ile Asp Glu Ile Tyr Leu  
 290 295 300  
 Lys Lys  
 305  
 45 <210> 211  
 <211> 246  
 <212> PRT  
 <213> Streptococcus pneumoniae  
 50 <400> 211  
 Met Glu Ile Ser Leu Leu Thr Asp Val Gly Gln Lys Arg Thr Asn Asn  
 1 5 10 15  
 55 Gln Asp Tyr Val Asn His Tyr Val Asn Arg Ala Gly Arg Thr Met Ile  
 20 25 30



165

Ile Ser Ile Gly Gly Asp Gly Met Leu Leu Ser Ala Phe His Lys Tyr  
 50 55 60  
 5 Glu Asn Gln Leu Asp Lys Val Arg Phe Ile Gly Leu His Thr Gly His  
 65 70 75 80  
 Leu Gly Phe Tyr Thr Asp Tyr Arg Asp Phe Glu Leu Asp Lys Leu Val  
 85 90 95  
 10 Thr Asn Leu Gln Leu Asp Thr Gly Ala Arg Val Ser Tyr Pro Val Leu  
 100 105 110  
 15 Asn Val Lys Val Phe Leu Glu Asn Gly Glu Val Lys Ile Phe Arg Ala  
 115 120 125  
 Leu Asn Glu Ala Ser Ile Arg Arg Ser Asp Arg Thr Met Val Ala Asp  
 130 135 140  
 20 Ile Val Ile Asn Gly Val Pro Phe Glu Arg Phe Arg Gly Asp Gly Leu  
 145 150 155 160  
 Thr Val Ser Thr Pro Thr Gly Ser Thr Ala Tyr Asn Lys Ser Leu Gly  
 165 170 175  
 25 Gly Ala Val Leu His Pro Thr Ile Glu Ala Leu Gln Leu Thr Glu Ile  
 180 185 190  
 30 Ala Ser Leu Asn Asn Arg Val Tyr Arg Thr Leu Gly Ser Ser Ile Ile  
 195 200 205  
 Val Pro Lys Lys Asp Lys Ile Glu Leu Ile Pro Thr Arg Asn Asp Tyr  
 210 215 220  
 35 His Thr Ile Ser Val Asp Asn Ser Val Tyr Ser Phe Arg Asn Ile Glu  
 225 230 235 240  
 Arg Ile Glu Tyr Gln Ile Asp His His Lys Ile His Phe Val Ala Thr  
 245 250 255  
 40 Pro Ser His Thr Ser Phe Trp Asn Arg Val Lys Asp Ala Phe Ile Gly  
 260 265 270  
 45 Glu Val Asp Glu  
 275  
 <210> 213  
 <211> 540  
 50 <212> PRT  
 <213> Streptococcus pneumoniae  
 <400> 213  
 55 Met Ser Lys Glu Ile Lys Phe Ser Ser Asp Ala Arg Ser Ala Met Val  
 1 5 10 15  
 Arg Gly Val Asp Ile Leu Ala Asp Thr Val Lys Val Thr Leu Gly Pro

	20	25	30
	Lys Gly Arg Asn Val Val Leu Glu Lys Ser Phe Gly Ser Pro Leu Ile		
	35	40	45
5	Thr Asn Asp Gly Val Thr Ile Ala Lys Glu Ile Glu Leu Glu Asp His		
	50	55	60
10	Phe Glu Asn Met Gly Ala Lys Leu Val Ser Glu Val Ala Ser Lys Thr		
	65	70	75
	Asn Asp Ile Ala Gly Asp Gly Thr Thr Thr Ala Thr Val Leu Thr Gln		
	85	90	95
15	Ala Ile Val Arg Glu Gly Ile Lys Asn Val Thr Ala Gly Ala Asn Pro		
	100	105	110
	Ile Gly Ile Arg Arg Gly Ile Glu Thr Ala Val Ala Ala Val Glu		
	115	120	125
20	Ala Leu Lys Asn Asn Ala Ile Pro Val Ala Asn Lys Glu Ala Ile Ala		
	130	135	140
	Gln Val Ala Ala Val Ser Ser Arg Ser Glu Lys Val Gly Glu Tyr Ile		
25	145	150	155
	Ser Glu Ala Met Glu Lys Val Gly Lys Asp Gly Val Ile Thr Ile Glu		
	165	170	175
30	Glu Ser Arg Gly Met Glu Thr Glu Leu Glu Val Val Glu Gly Met Gln		
	180	185	190
	Phe Asp Arg Gly Tyr Leu Ser Gln Tyr Met Val Thr Asp Ser Glu Lys		
	195	200	205
35	Met Val Ala Asp Leu Glu Asn Pro Tyr Ile Leu Ile Thr Asp Lys Lys		
	210	215	220
	Ile Ser Asn Ile Gln Glu Ile Leu Pro Leu Leu Glu Ser Ile Leu Gln		
40	225	230	235
	Ser Asn Arg Pro Leu Leu Ile Ile Ala Asp Asp Val Asp Gly Glu Ala		
	245	250	255
45	Leu Pro Thr Leu Val Leu Asn Lys Ile Arg Gly Thr Phe Asn Val Val		
	260	265	270
	Ala Val Lys Ala Pro Gly Phe Gly Asp Arg Arg Lys Ala Met Leu Glu		
	275	280	285
50	Asp Ile Ala Ile Leu Thr Gly Gly Thr Val Ile Thr Glu Asp Leu Gly		
	290	295	300
	Leu Glu Leu Lys Asp Ala Thr Ile Glu Ala Leu Gly Gln Ala Ala Arg		
55	305	310	315
	Val Thr Val Asp Lys Asp Ser Thr Val Ile Val Glu Gly Ala Gly Asn		

	325	330	335
	Pro Glu Ala Ile Ser His Arg Val Ala Val Ile Lys Ser Gln Ile Glu		
	340	345	350
5	Thr Thr Thr Ser Glu Phe Asp Arg Glu Lys Leu Gln Glu Arg Leu Ala		
	355	360	365
10	Lys Leu Ser Gly Gly Val Ala Val Ile Lys Val Gly Ala Ala Thr Glu		
	370	375	380
	Thr Glu Leu Lys Glu Met Lys Leu Arg Ile Glu Asp Ala Leu Asn Ala		
	385	390	395
15	Thr Arg Ala Ala Val Glu Glu Gly Ile Val Ala Gly Gly Gly Thr Ala		
	405	410	415
	Leu Ala Asn Val Ile Pro Ala Val Ala Thr Leu Glu Leu Thr Gly Asp		
	420	425	430
20	Glu Ala Thr Gly Arg Asn Ile Val Leu Arg Ala Leu Glu Glu Pro Val		
	435	440	445
	Arg Gln Ile Ala His Asn Ala Gly Phe Glu Gly Ser Ile Val Ile Asp		
	450	455	460
25	Arg Leu Lys Asn Ala Glu Leu Gly Ile Gly Phe Asn Ala Ala Thr Gly		
	465	470	475
			480
30	Glu Trp Val Asn Met Ile Asp Gln Gly Ile Ile Asp Pro Val Lys Val		
	485	490	495
	Ser Arg Ser Ala Leu Gln Asn Ala Ala Ser Val Ala Ser Leu Ile Leu		
	500	505	510
35	Thr Thr Glu Ala Val Val Ala Asn Lys Pro Glu Pro Val Ala Pro Ala		
	515	520	525
40	Pro Ala Met Asp Pro Ser Met Met Gly Gly Met Met		
	530	535	540
	<210> 214		
	<211> 481		
45	<212> PRT		
	<213> Streptococcus pneumoniae		
	<400> 214		
50	Met Ile Lys Ile Glu Thr Val Leu Asp Ile Leu Lys Lys Asp Gly Leu		
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			15
	Phe Arg Glu Ile Ile Asp Gln Gly His Tyr His Tyr Asn Tyr Ser Lys		
	20	25	30
55	Val Ile Phe Asp Ser Ile Ser Tyr Asp Ser Arg Lys Val Thr Glu Asp		
	35	40	45

Thr Leu Phe Phe Ala Lys Gly Ala Ala Phe Lys Lys Glu Tyr Leu Leu  
 50 55 60  
 5 Ser Ala Ile Thr Gln Gly Leu Ala Trp Tyr Val Ala Glu Lys Asp Tyr  
 65 70 75 80  
 Glu Val Gly Ile Pro Val Ile Ile Val Asn Asp Ile Lys Lys Ala Met  
 85 90 95  
 10 Ser Leu Ile Ala Met Glu Phe Tyr Gly Asn Pro Gln Glu Lys Leu Lys  
 100 105 110  
 Leu Leu Ala Phe Thr Gly Thr Lys Gly Lys Thr Thr Ala Ala Tyr Phe  
 115 120 125  
 15 Ala Tyr Asn Ile Leu Ser Gln Gly His Arg Pro Ala Met Leu Ser Thr  
 130 135 140  
 20 Met Asn Thr Thr Leu Asp Gly Glu Thr Phe Phe Lys Ser Ala Leu Thr  
 145 150 155 160  
 Thr Pro Glu Ser Ile Asp Leu Phe Asp Met Met Asn Gln Ala Val Gln  
 165 170 175  
 25 Asn Asp Arg Thr His Leu Ile Met Glu Val Ser Ser Gln Ala Tyr Leu  
 180 185 190  
 Val Lys Arg Val Tyr Gly Leu Thr Phe Asp Val Gly Val Phe Leu Asn  
 195 200 205  
 30 Ile Ser Pro Asp His Ile Gly Pro Ile Glu His Pro Ser Phe Glu Asp  
 210 215 220  
 35 Tyr Phe Tyr His Lys Arg Leu Leu Met Glu Lys Ser Arg Ala Val Ile  
 225 230 235 240  
 Ile Asn Ser Asp Met Asp His Phe Ser Val Leu Lys Glu Gln Val Glu  
 245 250 255  
 40 Asp Gln Asp His Asp Phe Tyr Gly Ser Gln Phe Asp Asn Gln Ile Glu  
 260 265 270  
 Asn Ser Lys Ala Phe Ser Phe Ser Ala Thr Gly Lys Leu Ala Gly Asp  
 275 280 285  
 45 Tyr Asp Ile Gln Leu Ile Gly Asn Phe Asn Gln Glu Asn Ala Val Ala  
 290 295 300  
 50 Ala Gly Leu Ala Cys Leu Arg Leu Gly Ala Ser Leu Glu Asp Ile Lys  
 305 310 315 320  
 Lys Gly Ile Ala Ala Thr Arg Val Pro Gly Arg Met Glu Val Leu Thr  
 325 330 335  
 55 Gln Lys Asn Gly Ala Lys Val Phe Ile Asp Tyr Ala His Asn Gly Asp  
 340 345 350

Ser Leu Lys Lys Leu Ile Asn Val Val Glu Thr His Gln Thr Gly Lys  
 355 360 365  
 5 Ile Ala Leu Val Leu Gly Ser Thr Gly Asn Lys Gly Glu Ser Arg Arg  
 370 375 380  
 Lys Asp Phe Gly Leu Leu Leu Asn Gln His Pro Glu Ile Gln Val Phe  
 385 390 395 400  
 10 Leu Thr Ala Asp Asp Pro Asn Tyr Glu Asp Pro Met Ala Ile Ala Asp  
 405 410 415  
 Glu Ile Ser Ser Tyr Ile Asn His Pro Val Glu Lys Ile Ala Asp Arg  
 420 425 430  
 15 Gln Glu Ala Ile Lys Ala Ala Met Ala Ile Thr Asn His Glu Leu Asp  
 435 440 445  
 Ala Val Ile Ile Ala Gly Lys Gly Ala Asp Cys Tyr Gln Ile Ile Gln  
 20 450 455 460  
 Gly Lys Lys Glu Ser Tyr Pro Gly Asp Thr Ala Val Ala Glu Asn Tyr  
 465 470 475 480  
 25 Leu  
 30 <210> 215  
 <211> 659  
 <212> PRT  
 <213> Streptococcus pneumoniae  
 <400> 215  
 35 Met Ile Gln Ile Gly Lys Ile Phe Ala Gly Arg Tyr Arg Ile Val Lys  
 1 5 10 15  
 Gln Ile Gly Arg Gly Gly Met Ala Asp Val Tyr Leu Ala Lys Asp Leu  
 20 25 30  
 40 Ile Leu Asp Gly Glu Glu Val Ala Val Lys Val Leu Arg Thr Asn Tyr  
 35 40 45  
 Gln Thr Asp Pro Ile Ala Val Ala Arg Phe Gln Arg Glu Ala Arg Ala  
 45 50 55 60  
 Met Ala Asp Leu Asp His Pro His Ile Val Arg Ile Thr Asp Ile Gly  
 65 70 75 80  
 50 Glu Glu Asp Gly Gln Gln Tyr Leu Ala Met Glu Tyr Val Ala Gly Leu  
 85 90 95  
 Asp Leu Lys Arg Tyr Ile Lys Glu His Tyr Pro Leu Ser Asn Glu Glu  
 100 105 110  
 55 Ala Val Arg Ile Met Gly Gln Ile Leu Leu Ala Met Arg Leu Ala His  
 115 120 125

Thr Arg Gly Ile Val His Arg Asp Leu Lys Pro Gln Asn Ile Leu Leu  
 130 135 140  
 5 Thr Pro Asp Gly Thr Ala Lys Val Thr Asp Phe Gly Ile Ala Val Ala  
 145 150 155 160  
 Phe Ala Glu Thr Ser Leu Thr Gln Thr Asn Ser Met Leu Gly Ser Val  
 165 170 175  
 10 His Tyr Leu Ser Pro Glu Gln Ala Arg Gly Ser Lys Ala Thr Val Gln  
 180 185 190  
 Ser Asp Ile Tyr Ala Met Gly Ile Ile Phe Tyr Glu Met Leu Thr Gly  
 195 200 205  
 15 His Ile Pro Tyr Asp Gly Asp Ser Ala Val Thr Ile Ala Leu Gln His  
 210 215 220  
 20 Phe Gln Lys Pro Leu Pro Ser Val Ile Ala Glu Asn Pro Ser Val Pro  
 225 230 235 240  
 Gln Ala Leu Glu Asn Val Ile Ile Lys Ala Thr Ala Lys Lys Leu Thr  
 245 250 255  
 25 Asn Arg Tyr Arg Ser Val Ser Glu Met Tyr Val Asp Leu Ser Ser Ser  
 260 265 270  
 30 Leu Ser Tyr Asn Arg Arg Asn Glu Ser Lys Leu Ile Phe Asp Glu Thr  
 275 280 285  
 Ser Lys Ala Asp Thr Lys Thr Leu Pro Lys Val Ser Gln Ser Thr Leu  
 290 295 300  
 35 Thr Ser Ile Pro Lys Val Gln Ala Gln Thr Glu His Lys Ser Ile Lys  
 305 310 315 320  
 Asn Pro Ser Gln Ala Val Thr Glu Glu Thr Tyr Gln Pro Gln Ala Pro  
 325 330 335  
 40 Lys Lys His Arg Phe Lys Met Arg Tyr Leu Ile Leu Leu Ala Ser Leu  
 340 345 350  
 Val Leu Val Ala Ala Ser Leu Ile Trp Ile Leu Ser Arg Thr Pro Ala  
 355 360 365  
 45 Thr Ile Ala Ile Pro Asp Val Ala Gly Gln Thr Val Ala Glu Ala Lys  
 370 375 380  
 50 Ala Thr Leu Lys Lys Ala Asn Phe Glu Ile Gly Glu Glu Lys Thr Glu  
 385 390 395 400  
 Ala Ser Glu Lys Val Glu Glu Gly Arg Ile Ile Arg Thr Asp Pro Gly  
 405 410 415  
 55 Ala Gly Thr Gly Arg Lys Glu Gly Thr Lys Ile Asn Leu Val Val Ser  
 420 425 430

Ser Gly Lys Gln Ser Phe Gln Ile Ser Asn Tyr Val Gly Arg Lys Ser  
 435 440 445  
 5 Ser Asp Val Ile Ala Glu Leu Lys Glu Lys Lys Val Pro Asp Asn Leu  
 450 455 460  
 Ile Lys Ile Glu Glu Glu Glu Ser Asn Glu Ser Glu Ala Gly Thr Val  
 465 470 475 480  
 10 Leu Lys Gln Ser Leu Pro Glu Gly Thr Thr Tyr Asp Leu Ser Lys Ala  
 485 490 495  
 15 Thr Gln Ile Val Leu Thr Val Ala Lys Lys Ala Thr Thr Ile Gln Leu  
 500 505 510  
 Gly Asn Tyr Ile Gly Arg Asn Ser Thr Glu Val Ile Ser Glu Leu Lys  
 515 520 525  
 20 Gln Lys Lys Val Pro Glu Asn Leu Ile Lys Ile Glu Glu Glu Glu Ser  
 530 535 540  
 Ser Glu Ser Glu Pro Gly Thr Ile Met Lys Gln Ser Pro Gly Ala Gly  
 545 550 555 560  
 25 Thr Thr Tyr Asp Val Ser Lys Pro Thr Gln Ile Val Leu Thr Val Ala  
 565 570 575  
 Lys Lys Val Thr Ser Val Ala Met Pro Ser Tyr Ile Gly Ser Ser Leu  
 580 585 590  
 30 Glu Phe Thr Lys Asn Asn Leu Ile Gln Ile Val Gly Ile Lys Glu Ala  
 595 600 605  
 35 Asn Ile Glu Val Val Glu Val Thr Thr Ala Pro Ala Gly Ser Ala Glu  
 610 615 620  
 Gly Met Val Val Glu Gln Ser Pro Arg Ala Gly Glu Lys Val Asp Leu  
 625 630 635 640  
 40 Asn Lys Thr Arg Val Lys Ile Ser Ile Tyr Lys Pro Lys Thr Thr Ser  
 645 650 655  
 45 Ala Thr Pro  
 <210> 216  
 <211> 391  
 50 <212> PRT  
 <213> Streptococcus pneumoniae  
 <400> 216  
 Met Lys His Phe Asp Thr Ile Val Ile Gly Gly Gly Pro Ala Gly Met  
 55 1 5 10 15  
 Met Ala Thr Ile Ser Ser Asn Phe Tyr Gly Gln Lys Thr Leu Leu Ile



	20	25	30
	Glu Lys Asn Arg Lys Leu Gly Lys Lys Leu Ala Gly Thr Gly Gly Gly		
	35	40	45
5	Arg Cys Asn Val Thr Asn Asn Gly Ser Leu Asp Asn Leu Leu Ala Gly		
	50	55	60
	Ile Pro Gly Asn Gly Arg Phe Leu Tyr Ser Val Phe Ser Gln Phe Asp		
10	65	70	75 80
	Asn His Asp Ile Ile Asn Phe Phe Thr Glu Asn Gly Val Lys Leu Lys		
	85	90	95
15	Val Glu Asp His Gly Arg Val Phe Pro Ala Ser Asp Lys Ser Arg Thr		
	100	105	110
	Ile Ile Glu Ala Leu Glu Lys Lys Ile Thr Glu Leu Gly Gly Gln Val		
	115	120	125
20	Ala Thr Gln Ile Glu Ile Val Ser Val Lys Lys Val Asp Asp Gln Phe		
	130	135	140
	Val Leu Lys Ser Ala Asp Gln Thr Phe Thr Cys Glu Lys Leu Ile Val		
25	145	150	155 160
	Thr Thr Gly Gly Lys Ser Tyr Pro Ser Thr Gly Ser Thr Gly Phe Gly		
	165	170	175
30	His Glu Ile Ala Arg His Phe Lys His Thr Ile Thr Asp Leu Glu Ala		
	180	185	190
	Ala Glu Ser Pro Leu Leu Thr Asp Phe Pro His Lys Ala Leu Gln Gly		
	195	200	205
35	Ile Ser Leu Asp Asp Val Thr Leu Ser Tyr Gly Lys His Val Ile Thr		
	210	215	220
	His Asp Leu Leu Phe Thr His Phe Gly Leu Ser Gly Pro Ala Ala Leu		
40	225	230	235 240
	Arg Met Ser Ser Phe Val Lys Gly Gly Glu Val Leu Ser Leu Asp Val		
	245	250	255
45	Leu Pro Gln Leu Ser Glu Lys Asp Leu Val Thr Phe Leu Glu Glu Asn		
	260	265	270
	Arg Glu Lys Ser Leu Lys Asn Ala Leu Lys Thr Leu Leu Pro Glu Arg		
	275	280	285
50	Leu Ala Glu Phe Phe Val Gln Gly Tyr Pro Glu Lys Val Lys Gln Leu		
	290	295	300
	Thr Glu Lys Glu Arg Glu Gln Leu Val Gln Ser Ile Lys Glu Leu Lys		
55	305	310	315 320
	Ile Pro Val Thr Gly Lys Met Ser Leu Ala Lys Ser Phe Val Thr Lys		

174

Ala Tyr Val Glu His Val Leu Pro Glu Lys Met Arg Tyr Asn Leu Ala  
 195 200 205

5 Tyr Leu Arg Glu Phe Ser Phe Phe Gly Asp Ile Lys Ile Met Phe Gln  
 210 215 220

Thr Val Phe Glu Val Leu Lys  
 225 230

10 <210> 218  
 <211> 140  
 <212> PRT  
 <213> Streptococcus pneumoniae

15 <400> 218  
 Met Thr Ser Pro Leu Leu Glu Ser Arg Arg Gln Leu Arg Lys Cys Ala  
 1 5 10 15

20 Phe Gln Ala Leu Met Ser Leu Glu Phe Gly Thr Asp Val Glu Thr Ala  
 20 25 30

Cys Arg Phe Ala Tyr Thr His Asp Arg Glu Tyr Thr Asp Val Gln Leu  
 35 40 45

25 Pro Ala Phe Leu Ile Asp Leu Val Ser Gly Val Gln Ala Lys Lys Glu  
 50 55 60

30 Glu Leu Asp Lys Gln Ile Thr Gln His Leu Lys Ala Gly Trp Thr Ile  
 65 70 75 80

Glu Arg Leu Thr Leu Val Glu Arg Asn Leu Leu Arg Leu Gly Val Phe  
 85 90 95

35 Glu Ile Thr Ser Phe Asp Thr Pro Gln Leu Val Ala Val Asn Glu Ala  
 100 105 110

Ile Glu Leu Ala Lys Asp Phe Ser Asp Gln Lys Ser Ala Arg Phe Ile  
 115 120 125

40 Asn Gly Leu Leu Ser Gln Phe Val Thr Glu Glu Gln  
 130 135 140

45 <210> 219  
 <211> 1179  
 <212> PRT  
 <213> Streptococcus pneumoniae

50 <400> 219  
 Met Tyr Leu Lys Glu Ile Glu Ile Gln Gly Phe Lys Ser Phe Ala Asp  
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55 Lys Thr Lys Val Val Phe Asp Gln Gly Val Thr Ala Val Val Gly Pro  
 20 25 30

Asn Gly Ser Gly Lys Ser Asn Ile Thr Glu Ser Leu Arg Trp Ala Leu

	35	40	45
	Gly Glu Ser Ser Val Lys Ser Leu Arg Gly Gly Lys Met Pro Asp Val		
	50	55	60
5	Ile Phe Ala Gly Thr Glu Ser Arg Lys Pro Leu Asn Tyr Ala Ser Val		
	65	70	75 80
10	Val Val Thr Leu Asp Asn His Asp Gly Phe Ile Lys Asp Ala Gly Gln		
	85	90	95
	Glu Ile Arg Val Glu Arg His Ile Tyr Arg Ser Gly Asp Ser Glu Tyr		
	100	105	110
15	Lys Ile Asp Gly Lys Lys Val Arg Leu Arg Asp Ile His Asp Leu Phe		
	115	120	125
20	Leu Asp Thr Gly Leu Gly Arg Asp Ser Phe Ser Ile Ile Ser Gln Gly		
	130	135	140
	Lys Val Glu Glu Ile Phe Asn Ser Lys Pro Glu Glu Arg Arg Ala Ile		
	145	150	155 160
25	Phe Glu Glu Ala Ala Gly Val Leu Lys Tyr Lys Thr Arg Arg Lys Glu		
	165	170	175
	Thr Glu Ser Lys Leu Gln Gln Thr Gln Asp Asn Leu Asp Arg Leu Glu		
	180	185	190
30	Asp Ile Ile Tyr Glu Leu Asp Asn Gln Ile Lys Pro Leu Glu Lys Gln		
	195	200	205
	Ala Glu Asn Ala Arg Lys Phe Leu Asp Leu Glu Gly Gln Arg Lys Ala		
	210	215	220
35	Ile Tyr Leu Asp Val Leu Val Ala Gln Ile Lys Glu Asn Lys Ala Glu		
	225	230	235 240
40	Leu Glu Ser Thr Glu Glu Glu Leu Ala Gln Val Gln Glu Leu Leu Met		
	245	250	255
	Ser Tyr Tyr Gln Lys Arg Glu Lys Leu Glu Glu Glu Asn Gln Thr Leu		
	260	265	270
45	Lys Lys Gln Arg Gln Asp Leu Gln Ala Glu Met Ala Lys Asp Gln Gly		
	275	280	285
	Ser Leu Met Asp Leu Thr Ser Leu Ile Ser Asp Leu Glu Arg Lys Leu		
	290	295	300
50	Ala Leu Ser Lys Leu Glu Ser Glu Gln Val Ala Leu Asn Gln Gln Glu		
	305	310	315 320
55	Ala Gln Ala Arg Leu Ala Ala Leu Glu Asp Lys Arg Asn Ser Leu Ser		
	325	330	335
	Lys Glu Lys Tyr Asp Lys Glu Ser Ser Leu Ala Leu Leu Glu Gly Asn		

	340	345	350
	Leu Val Gln Asn Asn Gln Lys	Leu Asn Arg Leu Glu Ala Glu Leu Leu	
	355	360	365
5	Ala Phe Ser Asp Asp Pro Asp Gln Met Ile Glu Leu Leu Arg Glu Arg		
	370	375	380
10	Phe Val Ala Leu Leu Gln Glu Glu Ala Asp Val Ser Asn Gln Leu Thr		
	385	390	395
	Arg Ile Glu Asn Glu Leu Glu Asn Ser Arg Gln Leu Ser Gln Lys Gln		
	405	410	415
15	Ala Asp Gln Leu Glu Lys Leu Lys Glu Gln Leu Ala Thr Ala Lys Glu		
	420	425	430
	Lys Ala Ser Gln Gln Lys Asp Glu Leu Glu Thr Ala Lys Val Gln Val		
	435	440	445
20	Gln Lys Leu Leu Ala Asp Tyr Gln Ala Ile Ala Lys Glu Gln Glu Glu		
	450	455	460
25	Gln Lys Thr Ser Tyr Gln Ala Gln Gln Ser Gln Leu Phe Asp Arg Leu		
	465	470	475
	Asp Ser Leu Lys Asn Lys Gln Ala Arg Ala Gln Ser Leu Glu Asn Ile		
	485	490	495
30	Leu Arg Asn His Ser Asn Phe Tyr Ala Gly Val Lys Ser Val Leu Gln		
	500	505	510
	Glu Lys Asp Arg Leu Gly Gly Ile Ile Gly Ala Val Ser Glu His Leu		
	515	520	525
35	Thr Phe Asp Val Tyr Tyr Gln Thr Ala Leu Glu Ile Ala Leu Gly Ala		
	530	535	540
40	Ser Ser Gln His Ile Ile Val Glu Asp Glu Glu Ser Ala Thr Lys Ala		
	545	550	555
	Ile Asp Phe Leu Lys Arg Asn Arg Val Gly Arg Ala Thr Phe Leu Pro		
	565	570	575
45	Leu Thr Thr Ile Lys Ala Arg Thr Ile Ser Ser Gln Asn Gln Asp Ala		
	580	585	590
	Ile Ala Val Ser Pro Gly Phe Leu Gly Met Ala Asp Glu Leu Val Thr		
	595	600	605
50	Phe Asp Thr Arg Leu Glu Ala Ile Phe Lys Asn Leu Leu Ala Thr Thr		
	610	615	620
55	Ala Ile Phe Asp Thr Val Glu His Ala Arg Glu Ala Ala Arg Gln Val		
	625	630	635
	Arg Tyr Gln Val Arg Met Val Thr Leu Asp Gly Thr Glu Leu Arg Thr		

	645	650	655
	Gly Gly Ser Tyr Ala Gly Gly Ala Asn Arg Gln Asn Asn Ser Ile Phe		
	660	665	670
5	Ile Lys Pro Glu Leu Glu Gln Leu Gln Lys Glu Ile Ala Ala Asp Glu		
	675	680	685
10	Ala Ser Leu Gly Ser Glu Glu Ala Ala Leu Lys Thr Leu Gln Asp Gln		
	690	695	700
	Met Ala Ala Leu Thr Glu Arg Leu Glu Ala Ile Lys Ser Gln Gly Glu		
	705	710	715
15	Gln Ala Arg Ile Gln Glu Gln Gly Leu Ser Leu Ala Tyr Gln Gln Thr		
	725	730	735
	Ser Gln Gln Val Glu Glu Leu Glu Thr Leu Trp Lys Leu Gln Glu Glu		
	740	745	750
20	Glu Ile Asp Arg Leu Ser Glu Gly Asp Trp Gln Ala Asp Lys Glu Lys		
	755	760	765
25	Cys Gln Glu Ser Leu Ala Thr Ile Ala Ser Asp Lys Gln Asn Leu Glu		
	770	775	780
	Ala Glu Ile Glu Glu Ile Lys Ser Asn Lys Asn Ala Ile Gln Glu Arg		
	785	790	795
30	Tyr Gln Asn Leu Gln Glu Glu Val Ala Gln Ala Arg Leu Leu Lys Thr		
	805	810	815
	Lys Leu Gln Gly Gln Lys Arg Tyr Glu Val Ala Asp Ile Glu Arg Leu		
	820	825	830
35	Gly Lys Glu Leu Asp Asn Leu Asn Ile Glu Gln Glu Glu Ile Gln Arg		
	835	840	845
40	Met Leu Gln Glu Lys Val Asp Asn Leu Glu Lys Val Asp Thr Glu Leu		
	850	855	860
	Leu Ser Gln Gln Ala Glu Glu Ser Lys Thr Gln Lys Thr Asn Leu Gln		
	865	870	875
45	Gln Gly Leu Ile Arg Lys Gln Phe Glu Leu Asp Asp Ile Glu Gly Gln		
	885	890	895
	Leu Asp Asp Ile Ala Ser His Leu Asp Gln Ala Arg Gln Gln Asn Glu		
	900	905	910
50	Glu Trp Ile Arg Lys Gln Thr Arg Ala Glu Ala Lys Lys Glu Lys Val		
	915	920	925
55	Ser Glu Arg Leu Arg His Leu Gln Asn Gln Leu Thr Asp Gln Tyr Gln		
	930	935	940
	Ile Ser Tyr Thr Glu Ala Leu Glu Lys Ala His Glu Leu Glu Asn Leu		

945                      950                      955                      960  
 Asn Leu Ala Glu Gln Glu Val Gln Asp Leu Glu Lys Ala Ile Arg Ser  
                                  965                      970                      975  
 5 Leu Gly Pro Val Asn Leu Glu Ala Ile Asp Gln Tyr Glu Glu Val His  
                                  980                      985                      990  
 10 Asn Arg Leu Asp Phe Leu Asn Ser Gln Arg Asp Asp Ile Leu Ser Ala  
                                  995                      1000                      1005  
 Lys Asn Leu Leu Leu Glu Thr Ile Thr Glu Met Asn Asp Glu Val Lys  
                                  1010                      1015                      1020  
 15 Glu Arg Phe Lys Ser Thr Phe Glu Ala Ile Arg Glu Ser Phe Lys Val  
                                  1025                      1030                      1035                      1040  
 Thr Phe Lys Gln Met Phe Gly Gly Gly Gln Ala Asp Leu Ile Leu Thr  
                                  1045                      1050                      1055  
 20 Glu Gly Asp Leu Leu Thr Ala Gly Val Glu Ile Ser Val Gln Pro Pro  
                                  1060                      1065                      1070  
 25 Gly Lys Lys Ile Gln Ser Leu Asn Leu Met Ser Gly Gly Glu Lys Ala  
                                  1075                      1080                      1085  
 Leu Ser Ala Leu Ala Leu Leu Phe Ser Ile Ile Arg Val Lys Thr Ile  
                                  1090                      1095                      1100  
 30 Pro Phe Val Ile Leu Asp Glu Val Glu Ala Ala Leu Asp Glu Ala Asn  
                                  1105                      1110                      1115                      1120  
 Val Lys Arg Phe Gly Asp Tyr Leu Asn Arg Phe Asp Lys Asp Ser Gln  
                                  1125                      1130                      1135  
 35 Phe Ile Val Val Thr His Arg Lys Gly Thr Met Ala Ala Ala Asp Ser  
                                  1140                      1145                      1150  
 40 Ile Tyr Gly Val Thr Met Gln Glu Ser Gly Val Ser Lys Ile Val Ser  
                                  1155                      1160                      1165  
 Val Lys Leu Lys Asp Leu Glu Ser Ile Glu Gly  
                                  1170                      1175  
 45 <210> 220  
       <211> 447  
       <212> PRT  
       <213> Streptococcus pneumoniae  
 50 <400> 220  
 Met Thr Lys Arg Val Thr Ile Ile Asp Val Lys Asp Tyr Val Gly Gln  
       1                      5                      10                      15  
 55 Glu Val Thr Ile Gly Ala Trp Val Ala Asn Lys Ser Gly Lys Gly Lys  
                                  20                      25                      30

Ile Ala Phe Leu Gln Leu Arg Asp Gly Thr Ala Phe Phe Gln Gly Val  
                   35                                  40                                  45

5   Ala Phe Lys Pro Asn Phe Val Glu Lys Phe Gly Glu Glu Val Gly Leu  
       50                                  55                                  60

Glu Lys Phe Asp Val Ile Lys Arg Leu Ser Gln Glu Thr Ser Val Tyr  
   65                                  70                                  75                                  80

10   Val Thr Gly Ile Val Lys Glu Asp Glu Arg Ser Lys Phe Gly Tyr Glu  
                                   85                                  90                                  95

Leu Asp Ile Thr Asp Ile Glu Val Ile Gly Glu Ser Gln Asp Tyr Pro  
                                   100                                  105                                  110

15   Ile Thr Pro Lys Glu His Gly Thr Asp Phe Leu Met Asp Asn Arg His  
                                   115                                  120                                  125

20   Leu Trp Leu Arg Ser Arg Lys Gln Val Ala Val Leu Gln Ile Arg Asn  
       130                                  135                                  140

Ala Ile Ile Tyr Ala Thr Tyr Glu Phe Phe Asp Lys Asn Gly Phe Met  
   145                                  150                                  155                                  160

25   Lys Phe Asp Ser Pro Ile Leu Ser Gly Asn Ala Ala Glu Asp Ser Thr  
                                   165                                  170                                  175

Glu Leu Phe Glu Thr Asp Tyr Phe Gly Thr Pro Ala Tyr Leu Ser Gln  
                                   180                                  185                                  190

30   Ser Gly Gln Leu Tyr Leu Glu Ala Gly Ala Met Ala Leu Gly Arg Val  
                                   195                                  200                                  205

35   Phe Asp Phe Gly Pro Val Phe Arg Ala Glu Lys Ser Lys Thr Arg Arg  
       210                                  215                                  220

His Leu Thr Glu Phe Trp Met Met Asp Ala Glu Tyr Ser Tyr Leu Thr  
   225                                  230                                  235                                  240

40   His Asp Glu Ser Leu Asp Leu Gln Glu Ala Tyr Val Lys Ala Leu Leu  
                                   245                                  250                                  255

Gln Gly Val Leu Asp Arg Ala Pro Gln Ala Leu Glu Thr Leu Glu Arg  
                                   260                                  265                                  270

45   Asp Thr Glu Leu Leu Lys Arg Tyr Ile Ala Glu Pro Phe Lys Arg Ile  
                                   275                                  280                                  285

50   Thr Tyr Asp Gln Ala Ile Asp Leu Leu Gln Glu His Glu Asn Asp Glu  
       290                                  295                                  300

Asp Ala Asp Tyr Glu His Leu Glu His Gly Asp Asp Phe Gly Ser Pro  
   305                                  310                                  315                                  320

55   His Glu Thr Trp Ile Ser Asn His Phe Gly Val Pro Thr Phe Val Met  
                                   325                                  330                                  335



Asn Tyr Pro Ala Ala Ile Lys Ala Phe Tyr Met Lys Pro Val Pro Gly  
                             340                            345                            350  
 5 Asn Pro Glu Arg Val Leu Cys Ala Asp Leu Leu Ala Pro Glu Gly Tyr  
                             355                            360                            365  
 Gly Glu Ile Ile Gly Gly Ser Met Arg Glu Glu Asp Tyr Asp Ala Leu  
                             370                            375                            380  
 10 Val Ala Lys Met Asp Glu Leu Gly Met Asp Arg Thr Glu Tyr Glu Phe  
                             385                            390                            395                            400  
 Tyr Leu Asp Leu Arg Lys Tyr Gly Thr Val Pro His Gly Gly Phe Gly  
                             405                            410                            415  
 15 Ile Gly Ile Glu Arg Met Val Thr Phe Ala Ala Gly Thr Lys His Ile  
                             420                            425                            430  
 20 Arg Glu Ala Ile Pro Phe Pro Arg Met Leu His Arg Ile Lys Pro  
                             435                            440                            445  
 <210> 221  
 <211> 308  
 25 <212> PRT  
     <213> Streptococcus pneumoniae  
 <400> 221  
 30 Met Ser Glu Lys Leu Val Glu Ile Lys Asp Leu Glu Ile Ser Phe Gly  
     1                            5                            10                            15  
 Glu Gly Ser Lys Lys Phe Val Ala Val Lys Asn Ala Asn Phe Phe Ile  
                             20                            25                            30  
 35 Asn Lys Gly Glu Thr Phe Ser Leu Val Gly Glu Ser Gly Ser Gly Lys  
                             35                            40                            45  
 Thr Thr Ile Gly Arg Ala Ile Ile Gly Leu Asn Asp Thr Ser Asn Gly  
                             50                            55                            60  
 40 Asp Ile Ile Phe Asp Gly Gln Lys Ile Asn Gly Lys Lys Ser Arg Glu  
                             65                            70                            75                            80  
 Gln Ala Ala Glu Leu Ile Arg Arg Ile Gln Met Ile Phe Gln Asp Pro  
                             85                            90                            95  
 45 Ala Ala Ser Leu Asn Glu Arg Ala Thr Val Asp Tyr Ile Ile Ser Glu  
                             100                            105                            110  
 50 Gly Leu Tyr Asn His Arg Leu Phe Lys Asp Glu Glu Glu Arg Lys Glu  
                             115                            120                            125  
 Lys Val Gln Asn Ile Ile Arg Glu Val Gly Leu Leu Ala Glu His Leu  
                             130                            135                            140  
 55 Thr Arg Tyr Pro His Glu Phe Ser Gly Gly Gln Arg Gln Arg Ile Gly  
                             145                            150                            155                            160

Ile Ala Arg Ala Leu Val Met Gln Pro Asp Phe Val Ile Ala Asp Glu  
 165 170 175  
 5 Pro Ile Ser Ala Leu Asp Val Ser Val Arg Ala Gln Val Leu Asn Leu  
 180 185 190  
 Leu Lys Lys Phe Gln Lys Glu Leu Gly Leu Thr Tyr Leu Phe Ile Ala  
 195 200 205  
 10 His Asp Leu Ser Val Val Arg Phe Ile Ser Asp Arg Ile Ala Val Ile  
 210 215 220  
 Tyr Lys Gly Val Ile Val Glu Val Ala Glu Thr Glu Glu Leu Phe Asn  
 15 225 230 235 240  
 Asn Pro Ile His Pro Tyr Thr Gln Ala Leu Leu Ser Ala Val Pro Ile  
 245 250 255  
 20 Pro Asp Pro Ile Leu Glu Arg Lys Lys Val Leu Lys Val Tyr Asp Pro  
 260 265 270  
 Ser Gln His Asp Tyr Glu Thr Asp Lys Pro Ser Met Val Glu Ile Arg  
 275 280 285  
 25 Pro Gly His Tyr Val Trp Ala Asn Gln Thr Glu Leu Ala Arg Tyr Gln  
 290 295 300  
 Lys Gly Leu Asn  
 30 305  
 <210> 222  
 <211> 424  
 35 <212> PRT  
 <213> Streptococcus pneumoniae  
 <400> 222  
 Met Lys Ile Ser Trp Asn Gly Phe Ser Lys Lys Ser Tyr Gln Glu Arg  
 40 1 5 10 15  
 Leu Glu Leu Leu Lys Ala Gln Ala Leu Leu Ser Pro Glu Arg Gln Ala  
 20 25 30  
 45 Ser Leu Glu Lys Asp Glu Gln Met Ser Val Thr Val Ala Asp Gln Leu  
 35 40 45  
 Ser Glu Asn Val Val Gly Thr Phe Ser Leu Pro Tyr Ser Leu Val Pro  
 50 55 60  
 50 Glu Val Leu Val Asn Gly Gln Glu Tyr Thr Val Pro Tyr Val Thr Glu  
 65 70 75 80  
 Glu Pro Ser Val Val Ala Ala Ala Ser Tyr Ala Ser Lys Ile Ile Lys  
 55 85 90 95  
 Arg Ala Gly Gly Phe Thr Ala Gln Val His Gln Arg Gln Met Ile Gly

	100	105	110
	Gln Val Ala Leu Tyr Gln Ile Ala Asn Pro Lys Leu Ala Gln Glu Lys		
	115	120	125
5	Ile Ala Ser Lys Lys Ala Glu Leu Leu Glu Leu Ala Asn Gln Ala Tyr		
	130	135	140
10	Pro Ser Ile Val Lys Arg Gly Gly Gly Ala Arg Asp Leu His Val Glu		
	145	150	155
	Gln Ile Lys Gly Glu Pro Asp Phe Leu Val Val Tyr Ile His Val Asp		
	165	170	175
15	Thr Gln Glu Ala Met Gly Ala Asn Met Leu Asn Thr Met Leu Glu Ala		
	180	185	190
	Leu Lys Pro Val Leu Glu Glu Leu Ser Gln Gly Gln Ser Leu Met Gly		
	195	200	205
20	Ile Leu Ser Asn Tyr Ala Thr Asp Ser Leu Val Thr Ala Ser Cys Arg		
	210	215	220
25	Ile Ala Phe Arg Tyr Leu Ser Arg Gln Lys Asp Gln Gly Arg Glu Ile		
	225	230	235
	Ala Glu Lys Ile Ala Leu Ala Ser Gln Phe Ala Gln Ala Asp Pro Tyr		
	245	250	255
30	Arg Ala Ala Thr His Asn Lys Gly Ile Phe Asn Gly Ile Asp Ala Ile		
	260	265	270
	Leu Ile Ala Thr Gly Asn Asp Trp Arg Ala Ile Glu Ala Gly Ala His		
	275	280	285
35	Ala Phe Ala Ser Arg Asp Gly Arg Tyr Gln Gly Leu Ser Cys Trp Thr		
	290	295	300
40	Leu Asp Leu Glu Arg Glu Glu Leu Val Gly Glu Met Thr Leu Pro Met		
	305	310	315
	Pro Val Ala Thr Lys Gly Gly Ser Ile Gly Leu Asn Pro Arg Val Ala		
	325	330	335
45	Leu Ser His Asp Leu Leu Gly Asn Pro Ser Ala Arg Glu Leu Ala Gln		
	340	345	350
	Ile Ile Val Ser Ile Gly Leu Ala Gln Asn Phe Ala Ala Leu Lys Ala		
	355	360	365
50	Leu Val Ser Thr Gly Ile Gln Gln Gly His Met Lys Leu Gln Ala Lys		
	370	375	380
55	Ser Leu Ala Leu Leu Ala Gly Ala Ser Glu Ser Glu Val Ala Pro Leu		
	385	390	395
	Val Glu Arg Leu Ile Ser Asp Lys Thr Phe Asn Leu Glu Thr Ala Gln		
			400

405                      410                      415  
 Arg Tyr Leu Glu Asn Leu Arg Ser  
 420  
 5  
 <210> 223  
 <211> 262  
 <212> PRT  
 10 <213> Streptococcus pneumoniae  
 <400> 223  
 Met Pro Ile Thr Ser Leu Glu Ile Lys Asp Lys Thr Phe Gly Thr Arg  
 1                      5                      10                      15  
 15 Phe Arg Gly Phe Asp Pro Glu Glu Val Asp Glu Phe Leu Asp Ile Val  
 20                      20                      25                      30  
 Val Arg Asp Tyr Glu Asp Leu Val Arg Ala Asn His Asp Lys Asn Leu  
 20                      35                      40                      45  
 Arg Ile Lys Ser Leu Glu Glu Arg Leu Ser Tyr Phe Asp Glu Ile Lys  
 50                      55                      60  
 25 Asp Ser Leu Ser Gln Ser Val Leu Ile Ala Gln Asp Thr Ala Glu Arg  
 65                      70                      75                      80  
 Val Lys Gln Ala Ala His Glu Arg Ser Asn Asn Ile Ile His Gln Ala  
 85                      90                      95  
 30 Glu Gln Asp Ala Gln Arg Leu Leu Glu Glu Ala Lys Tyr Lys Ala Asn  
 100                      105                      110  
 Glu Ile Leu Arg Gln Ala Thr Asp Asn Ala Lys Lys Val Ala Val Glu  
 115                      120                      125  
 35 Thr Glu Glu Leu Lys Asn Lys Ser Arg Val Phe His Gln Arg Leu Lys  
 130                      135                      140  
 40 Ser Thr Ile Glu Ser Gln Leu Ala Ile Val Glu Ser Ser Asp Trp Glu  
 145                      150                      155                      160  
 Asp Ile Leu Arg Pro Thr Ala Thr Tyr Leu Gln Thr Ser Asp Glu Ala  
 165                      170                      175  
 45 Phe Lys Glu Val Val Ser Glu Val Leu Gly Glu Pro Ile Pro Ala Pro  
 180                      185                      190  
 50 Ile Glu Glu Glu Pro Ile Asp Met Thr Arg Gln Phe Ser Gln Ala Glu  
 195                      200                      205  
 Met Ala Glu Leu Gln Ala Arg Ile Glu Val Ala Asp Lys Glu Leu Ser  
 210                      215                      220  
 55 Glu Phe Glu Ala Gln Ile Lys Gln Glu Val Glu Ala Pro Thr Pro Val  
 225                      230                      235                      240

Val Ser Pro Gln Val Glu Glu Glu Pro Leu Leu Ile Gln Leu Ala Gln  
245 250 255

5 Cys Met Lys Asn Gln Lys  
260

10 <210> 224  
<211> 575  
<212> PRT  
<213> Streptococcus pneumoniae

15 <400> 224  
Met Ser Asn Gly Gln Leu Ile Tyr Leu Met Val Ala Ile Ala Val Ile  
1 5 10 15

Leu Val Leu Ala Tyr Val Val Ala Ile Phe Leu Arg Lys Arg Asn Glu  
20 25 30

20 Gly Arg Leu Glu Ala Leu Glu Glu Arg Lys Glu Glu Leu Tyr Asn Leu  
35 40 45

Pro Val Asn Asp Glu Val Glu Ala Val Lys Asn Met His Leu Ile Gly  
50 55 60

25 Gln Ser Gln Val Ala Phe Arg Glu Trp Asn Gln Lys Trp Val Asp Leu  
65 70 75 80

30 Ser Leu Asn Ser Phe Ala Asp Ile Glu Asn Asn Leu Phe Glu Ala Glu  
85 90 95

Gly Tyr Asn His Ser Phe Arg Phe Leu Lys Ala Ser His Gln Ile Asp  
100 105 110

35 Gln Ile Glu Ser Gln Ile Thr Leu Ile Glu Glu Asp Ile Ala Ala Ile  
115 120 125

Arg Asn Ala Leu Ala Asp Leu Glu Lys Gln Glu Ser Lys Asn Ser Gly  
130 135 140

40 Arg Val Leu His Ala Leu Asp Leu Phe Glu Glu Leu Gln His Arg Val  
145 150 155 160

45 Ala Glu Asn Ser Glu Gln Tyr Gly Gln Ala Leu Asp Glu Ile Glu Lys  
165 170 175

Gln Leu Glu Asn Ile Gln Ser Glu Phe Ser Gln Phe Val Thr Leu Asn  
180 185 190

50 Ser Ser Gly Asp Pro Val Glu Ala Ala Val Ile Leu Asp Asn Thr Glu  
195 200 205

Asn His Ile Leu Ala Leu Ser His Ile Val Asp Arg Val Pro Ala Leu  
210 215 220

55 Val Thr Thr Leu Ser Thr Glu Leu Pro Asp Gln Leu Gln Asp Leu Glu  
225 230 235 240

Ala Gly Tyr Arg Lys Leu Ile Asp Ala Asn Tyr His Phe Val Glu Thr  
245 250 255

5 Asp Ile Glu Ala Arg Phe His Leu Leu Tyr Glu Ala Phe Lys Lys Asn  
260 265 270

Gln Glu Asn Ile Arg Gln Leu Glu Leu Asp Asn Ala Glu Tyr Glu Asn  
275 280 285

10 Gly Gln Ala Gln Glu Glu Ile Asn Ala Leu Tyr Asp Ile Phe Thr Arg  
290 295 300

15 Glu Ile Ala Ala Gln Lys Val Val Glu Asn Leu Leu Ala Thr Leu Pro  
305 310 315 320

Thr Tyr Leu Gln His Met Lys Glu Asn Asn Thr Leu Leu Gly Glu Asp  
325 330 335

20 Ile Ala Arg Leu Asn Lys Thr Tyr Leu Leu Pro Glu Thr Ala Ala Ser  
340 345 350

His Val Arg Arg Ile Gln Thr Glu Leu Glu Ser Phe Glu Ala Ala Ile  
355 360 365

25 Val Glu Val Thr Ser Asn Gln Glu Glu Pro Thr Gln Ala Tyr Ser Val  
370 375 380

30 Leu Glu Glu Asn Leu Glu Asp Leu Gln Thr Gln Leu Lys Asp Ile Glu  
385 390 395 400

Asp Glu Gln Ile Ser Val Ser Glu Arg Leu Thr Gln Ile Glu Lys Asp  
405 410 415

35 Asp Ile Asn Ala Arg Gln Lys Ala Asn Val Tyr Val Asn Arg Leu His  
420 425 430

Thr Ile Lys Arg Tyr Met Glu Lys Arg Asn Leu Pro Gly Ile Pro Gln  
435 440 445

40 Thr Phe Leu Lys Leu Phe Phe Thr Ala Ser Asn Asn Thr Glu Asp Leu  
450 455 460

45 Met Val Glu Leu Glu Gln Lys Met Ile Asn Ile Glu Ser Val Thr Arg  
465 470 475 480

Val Leu Glu Ile Ala Thr Asn Asp Met Glu Ala Leu Glu Thr Glu Thr  
485 490 495

50 Tyr Asn Ile Val Gln Tyr Ala Thr Leu Thr Glu Gln Leu Leu Gln Tyr  
500 505 510

Ser Asn Arg Tyr Arg Ser Phe Asp Glu Arg Ile Gln Glu Ala Phe Asn  
515 520 525

55 Glu Ala Leu Asp Ile Phe Glu Lys Glu Phe Asp Tyr His Ala Ser Phe  
530 535 540

Asp Lys Ile Ser Gln Ala Leu Glu Val Ala Glu Pro Gly Val Thr Asn  
 545 550 555 560

5 Arg Phe Val Thr Ser Tyr Glu Lys Thr Arg Glu Thr Ile Arg Phe  
 565 570 575

10 <210> 225  
 <211> 800  
 <212> PRT  
 <213> Streptococcus pneumoniae

<400> 225

15 Met Leu Ile Ser Tyr Lys Trp Leu Lys Glu Leu Val Asp Ile Asp Val  
 1 5 10 15

Pro Ser Gln Glu Leu Ala Glu Lys Met Ser Thr Thr Gly Ile Glu Val  
 20 25 30

20 Glu Gly Val Glu Ser Pro Ala Ala Gly Leu Ser Lys Ile Val Val Gly  
 35 40 45

25 Glu Val Leu Ser Cys Glu Asp Val Pro Glu Thr His Leu His Val Cys  
 50 55 60

Gln Val Asn Val Gly Glu Glu Glu Arg Gln Ile Val Cys Gly Ala Pro  
 65 70 75 80

30 Asn Val Arg Ala Gly Ile Lys Val Met Val Ala Leu Pro Gly Ala Arg  
 85 90 95

Ile Ala Asp Asn Tyr Lys Ile Lys Lys Gly Lys Ile Arg Gly Leu Glu  
 100 105 110

35 Ser Leu Gly Met Ile Cys Ser Leu Gly Glu Leu Gly Ile Ser Asp Ser  
 115 120 125

40 Val Val Pro Lys Glu Phe Ala Asp Gly Ile Gln Ile Leu Pro Glu Asp  
 130 135 140

Ala Val Pro Gly Glu Glu Val Phe Ser Tyr Leu Asp Leu Asp Asp Glu  
 145 150 155 160

45 Ile Ile Glu Leu Ser Ile Thr Pro Asn Arg Ala Asp Ala Leu Ser Met  
 165 170 175

Cys Gly Val Ala His Glu Val Ala Ala Ile Tyr Asp Lys Ala Val Asn  
 180 185 190

50 Phe Lys Glu Phe Thr Leu Thr Glu Thr Asn Glu Ala Ala Ala Asp Ala  
 195 200 205

55 Leu Ser Val Ser Ile Glu Thr Asp Lys Ala Pro Tyr Tyr Ala Ala Arg  
 210 215 220

Ile Leu Asp Asn Val Thr Ile Ala Pro Ser Pro Gln Trp Leu Gln Asn

	225		230		235		240
	Leu Leu Met Asn Glu Gly Ile Arg Pro Ile Asn Asn Val Val Asp Val	245		250		255	
5	Thr Asn Tyr Ile Leu Leu Tyr Phe Gly Gln Pro Met His Ala Phe Asp	260		265		270	
10	Leu Asp Asn Phe Glu Gly Thr Asp Ile Arg Val Arg Glu Ala Arg Ala	275		280		285	
	Gly Glu Lys Leu Val Thr Leu Asp Gly Glu Glu Arg Asp Leu Asp Val	290		295		300	
15	Asn Asp Leu Val Ile Thr Val Ala Asp Lys Pro Val Ala Leu Ala Gly	305		310		315	320
20	Val Met Gly Gly Gln Ala Thr Glu Ile Ser Glu Lys Ser Ser Arg Val	325		330		335	
	Val Leu Glu Ala Ala Val Phe Asn Gly Lys Ser Ile Arg Lys Thr Ser	340		345		350	
25	Gly Arg Leu Asn Leu Arg Ser Glu Ser Ser Ser Arg Phe Glu Lys Gly	355		360		365	
	Ile Asn Val Ala Thr Val Asn Glu Ala Leu Asp Ala Ala Ala Ser Leu	370		375		380	
30	Ile Ala Glu Leu Ala Gly Ala Thr Val Arg Lys Gly Ile Val Ser Ala	385		390		395	400
35	Gly Glu Leu Asp Thr Ser Asp Val Glu Val Ser Ser Thr Leu Ala Asp	405		410		415	
	Val Asn Arg Val Leu Gly Thr Glu Leu Ser Tyr Ala Asp Val Glu Asp	420		425		430	
40	Val Phe Arg Arg Leu Gly Phe Gly Leu Ser Gly Asn Ala Asp Ser Phe	435		440		445	
	Thr Val Arg Val Pro Arg Arg Arg Trp Asp Ile Thr Ile Glu Ala Asp	450		455		460	
45	Leu Phe Glu Glu Ile Ala Arg Ile Tyr Gly Tyr Asp Arg Leu Pro Thr	465		470		475	480
50	Ser Leu Pro Lys Asp Asp Gly Thr Ala Gly Glu Leu Thr Ala Thr Gln	485		490		495	
	Lys Leu Arg Arg Gln Val Arg Thr Ile Ala Glu Gly Ala Gly Leu Thr	500		505		510	
55	Glu Ile Ile Thr Tyr Thr Leu Thr Thr Pro Glu Lys Ala Val Glu Phe	515		520		525	
	Thr Ala Gln Pro Ser Asn Leu Thr Glu Leu Met Trp Pro Met Thr Val						



530                      535                      540  
 Asp Arg Ser Val Leu Arg Gln Asn Met Ile Ser Gly Ile Leu Asp Thr  
 545                      550                      555                      560  
 5 Val Ala Tyr Asn Val Ala Arg Lys Asn Lys Asn Leu Ala Leu Tyr Glu  
                     565                      570                      575  
 10 Ile Gly Lys Val Phe Glu Gln Thr Gly Asn Pro Lys Glu Glu Leu Pro  
                     580                      585                      590  
 Asn Glu Ile Asn Ser Phe Ala Phe Ala Leu Thr Gly Leu Val Ala Glu  
                     595                      600                      605  
 15 Lys Asp Phe Gln Thr Ala Ala Val Pro Val Asp Phe Phe Tyr Ala Lys  
                     610                      615                      620  
 Gly Ile Leu Glu Ala Leu Phe Thr Arg Leu Gly Leu Gln Val Thr Tyr  
 20 625                      630                      635                      640  
 Thr Ala Thr Ser Glu Ile Ala Ser Leu His Pro Gly Arg Thr Ala Val  
                     645                      650                      655  
 25 Ile Ser Leu Gly Asp Gln Val Leu Gly Phe Leu Gly Gln Val His Pro  
                     660                      665                      670  
 Val Thr Ala Lys Ala Tyr Asp Ile Pro Glu Thr Tyr Val Ala Glu Leu  
                     675                      680                      685  
 30 Asn Leu Ser Ala Ile Glu Ala Ala Leu Gln Pro Ala Thr Pro Phe Val  
                     690                      695                      700  
 Glu Ile Thr Lys Phe Pro Ala Val Ser Arg Asp Val Ala Leu Leu Leu  
 35 705                      710                      715                      720  
 Lys Ala Glu Val Thr His Gln Glu Val Val Asp Ala Ile Gln Ala Ala  
                     725                      730                      735  
 40 Gly Val Lys Arg Leu Thr Asp Ile Lys Leu Phe Asp Val Phe Ser Gly  
                     740                      745                      750  
 Glu Lys Leu Gly Leu Gly Met Lys Ser Met Ala Tyr Ser Leu Thr Phe  
                     755                      760                      765  
 45 Gln Asn Pro Glu Asp Ser Leu Thr Asp Glu Glu Val Ala Arg Tyr Met  
                     770                      775                      780  
 Glu Lys Ile Gln Ala Ser Leu Glu Glu Lys Val Asn Ala Glu Val Arg  
 50 785                      790                      795                      800  
 55 <210> 226  
      <211> 180  
      <212> PRT

&lt;213&gt; Streptococcus pneumoniae

&lt;400&gt; 226

5 Met Leu Glu Asn Asp Ile Lys Lys Val Leu Val Ser His Asp Glu Ile  
    1                  5                  10                  15  
 Thr Glu Ala Ala Lys Lys Leu Gly Ala Gln Leu Thr Lys Asp Tyr Ala  
                   20                  25                  30  
 10 Gly Lys Asn Pro Ile Leu Val Gly Ile Leu Lys Gly Ser Ile Pro Phe  
                   35                  40                  45  
 Met Ala Glu Leu Val Lys His Ile Asp Thr His Ile Glu Met Asp Phe  
    50                  55                  60  
 15 Met Met Val Ser Ser Tyr His Gly Gly Thr Ala Ser Ser Gly Val Ile  
    65                  70                  75                  80  
 20 Asn Ile Lys Gln Asp Val Thr Gln Asp Ile Lys Gly Arg His Val Leu  
                   85                  90                  95  
 Phe Val Glu Asp Ile Ile Asp Thr Gly Gln Thr Leu Lys Asn Leu Arg  
                   100                  105                  110  
 25 Asp Met Phe Lys Ala Arg Glu Ala Ala Ser Val Lys Ile Ala Thr Leu  
                   115                  120                  125  
 Leu Asp Lys Pro Glu Gly Arg Val Val Glu Ile Glu Ala Asp Tyr Thr  
    130                  135                  140  
 30 Cys Phe Thr Ile Pro Asn Glu Phe Val Val Gly Tyr Gly Leu Asp Tyr  
    145                  150                  155                  160  
 35 Lys Glu Asn Tyr Arg Asn Leu Pro Tyr Ile Gly Val Leu Lys Glu Glu  
                   165                  170                  175  
 Val Tyr Ser Asn  
                   180

40